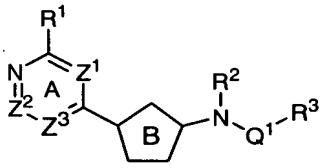
Applicants: Jingrong Cao et al.
Application No.: 10/696,862

## AMENDMENTS TO THE CLAIMS

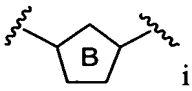
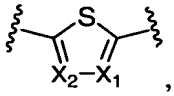
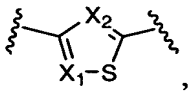
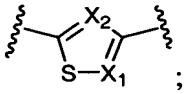
Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Currently amended) A compound of formula **I**:



(1) I

or a pharmaceutically acceptable salt thereof, wherein:

wherein  is  ,  , or  ;

$R^1$ is halogen, CN, $NO_2$, or $V_mR$;

$Z^1$ and $Z^3$ are each independently ~~N or~~ $CR^Z$, and $Z^2$ is ~~N or~~ $CR^1$~~, provided that Z1, Z2 and Z3 are not simultaneously N~~;

each occurrence of $R^Z$ is independently halogen, CN, $NO_2$, or $U_nR'$;

$R^2$ is $U_nR'$;

$X^1$ and $X^2$ are each independently $CR^4$ or N;

each occurrence of $R^4$ is independently halogen, CN, $NO_2$, or $V_mR$;

each occurrence of U or V is independently an optionally substituted $C_{1-6}$ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -$NRCO_2$-, -$SO_2NR$-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or -POR-;

m and n are each independently 0 or 1;

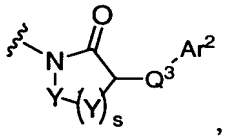
each occurrence of R is independently hydrogen or an optionally substituted $C_{1-6}$ aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted $C_{1-6}$ aliphatic group, a 3-8-membered saturated, partially

unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

$Q^1$ is –CO-, $-SO_2-$, -CONR-, or $–SO_2NR-$;

$R^3$ is $Q^2$-$Ar^1$,

or $R^2$ and $Q^1$-$R^3$, taken together with the nitrogen atom, form the cyclic group:



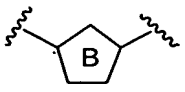
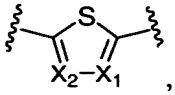
, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, $-SO_2-$, -O-, -S-, $-NR^5-$, or $-C(R^5)_2-$, and $R^5$ is $U_nR'$;

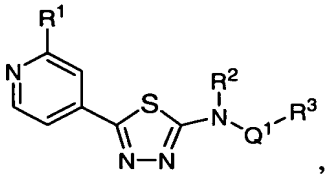
$Q^2$ and $Q^3$ are each independently a bond or a $C_{1-6}$ alkylidene chain, wherein up to two

methylene units of the chain are each optionally and independently replaced by –NR'-, -S-, -O-, -CS-, $-CO_2-$, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO-, $-NR'CO_2-$, $-SO_2NR'-$, $-NR'SO_2-$, -CONR'NR'-, -NR'CONR'-, -OCONR'-, -NR'NR'-, $-NR'SO_2NR'-$, -SO-, $-SO_2-$, -PO-, $-PO_2-$, or –POR'-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of $R^6$, wherein each occurrence of $R^6$ is independently halogen, CN, $NO_2$, or $U_nR'$, or two occurrences of $R^6$, or R' and $R^6$, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

$Ar^1$ and $Ar^2$ are each independently a 5-8 membered saturated, partially unsaturated, or

fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein $Ar^1$ and $Ar^2$ are each optionally substituted with 0-5 independent occurrences of $TR^7$; wherein T is a bond or is a $C_1$-$C_6$ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -$NRCO_2$-, -$SO_2NR$-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or -POR-; and each occurrence of $R^7$ is independently R', halogen, $NO_2$, or CN;
provided that:

I. for compounds described where  is  , one or more of, or all of the following conditions apply:

A) for compounds having the structure:  ,

i) when $R^1$ is Cl, and $R^2$ is –$CH(CH_3)COOCH_3$ or hydrogen, then $Q^1$-$R^3$ is not -CO(unsubstituted phenyl), -CO(unsubstituted 2-furyl), or -$COCH_2$(unsubstituted phenyl);

ii) when $R^1$ is hydrogen, $R^2$ is hydrogen, and $Q^1$ is –CO-, then $R^3$ is not:

a) phenyl substituted with 4–$O(CH_2)_{4\text{-}7}CH_3$ or 4–$(CH_2)_{4\text{-}7}CH_3$;;

b) phenyl subsituted with 2-Cl, 4-$NO_2$, 4-Cl, 2-Br, 3-Br, 3-I, 3-$CH_3$, 4-$OCH_3$, 3-$NO_2$, or 4-I;

c) 2,6-$OCH_3$-phenyl

d) (5-Cl, 3-$CH_3$, 1-phenyl)- pyrazol-4-yl; or

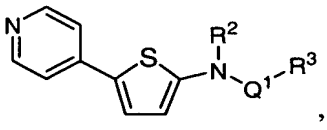
e) 4-OnBu-phenyl, -$CH_2O$(2-F-phenyl), -$(CH_2)_2$phenyl, furan-2-yl, thiophen-2-yl, 4-$CH_3$-phenyl, -$CH_2O$(2-$CH_3$-phenyl), 3-$OCH_3$-phenyl, 2-(2,5-dimethoxylphenyl)quinolin-4-yl, -NH-(4-Cl-phenyl), -NH-(3,4-dichlorophenyl), (2-$CO_2H$, 3-$NO_2$)-phenyl, 3,5-dimethyl-ixoxazol-4-yl, -CH=CH-phenyl, 4-F-phenyl, $C(CH_3)_2O$-(4-Cl-phenyl), -NH(3-Cl-phenyl), -NHphenyl, unsubstituted phenyl, 3,4,5-$OCH_3$-phenyl, 4-$NO_2$-phenyl, 4-cyclopentoxy-phenyl, -$(CH_2)_3$phenyl, -(tricyclo[3.3.1.13,7]decan-1-yl, -$CH_2O$-(3-$CH_3$-phenyl), 3-$NO_2$-phenyl, -cyclopropyl-(4-tert-butyl-phenyl), 2,3-$OCH_3$-phenyl, 1,3-benzodioxo-5-yl, -$CH_2$-O-(4-F-phenyl), or 3-Br-phenyl;

iii) when $R^1$ is hydrogen, $R^2$ is hydrogen, and $Q^1$ is –CSNH-, then $R^3$ is not 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl;

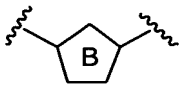
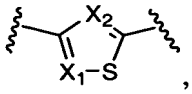
iv) when $R^1$ is hydrogen, $R^2$ is hydrogen, and $Q^1$ is $SO_2$, then $R^3$ is not unsubstituted phenyl, unsubstituted benzyl, unsubstituted naphthyl, phenyl substituted with para-$NHCOCH_3$, para-$NH_2$, or para-$CH_3$ ; and

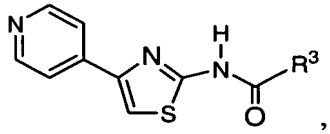
v) when $R^1$ is hydrogen, $R^2$ is $–CH_2CH=CH_2$, and $Q^1$ is CO, then $R^3$ is not 4-$OCH_3$-phenyl, unsubstituted naphthyl, -NH-(4-$OCH_3$-phenyl), 3,5-$OCH_3$-phenyl, -$CH_2O$phenyl, -$CH_2$-thiophen-2-yl, or –CH(phenyl)($CH_2CH_3$); and

vi) when $R^1$ is hydrogen, $R^2$ is $CH_2CH_3$, and $Q^1$ is CO, then $R^3$ is not 2,4-Cl-phenyl; and

B) for compounds having the structure: 

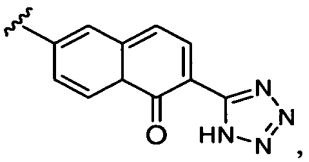
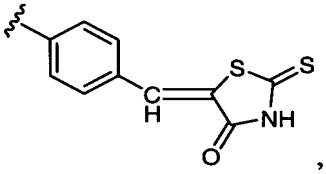
, when $R^2$ is hydrogen or $CH^3$, and $Q^1$ is –CO-, then $R^3$ is not $–OCH_2CH_2OCH_2$phenyl;

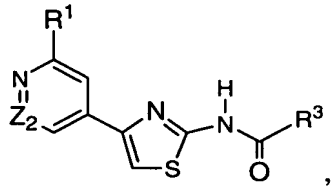
II. for compounds described where  is  , one or more of, or all of the following conditions apply:

A) for compounds having the structure:  ,

i) when $R^3$ is $Q^2$-$Ar^1$, and $Q^2$ is a bond then $Ar^1$ is not any one or more of the following: unsubstituted phenyl or phenyl substituted with 2-Br; 2-Cl; 2-I; 2,6-F; 3,5-$OCH_3$; 3,4,5-$OCH_3$; 2,4-$OCH_3$; 3,4-$CH_3$; 2,5-Cl; 3,4,-$OCH_3$; 2-Cl, 5-$NO_2$; 3,5-Cl; 3-$O(CH_2)_4CH_3$, 3-O-n-butyl, 3-$CF_3$, 3-$OCH_3$, 3-Br; 3-$NO_2$; 3-$CH_3$; 3-O-phenyl; 3-Cl; 4-$N(CH_3)_2$; 4-$N(CH_2CH_3)_2$; 4-$SO_2N(R')_2$; 4-CN; 4-$COOCH_3$; 4-C(O)phenyl; 4-phenyl; 4-tert-butyl, 4-O-phenyl; 4-O-isopropyl; 4-$OCH_3$; 4-$OCH_2CH_3$; 4-O-n-butyl; 4-Cl; 4-Br; 4-F; 4-$CH_3$; 4-$NO_2$; 4-Cl; 3-$NO_2$, 4-morpholino; 3-$NO_2$, 2,5-dioxopyrrolidinyl, or 4-piperidinyl; and

ii) $R^3$ is not any one or more of the following groups:

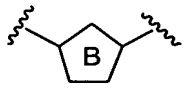
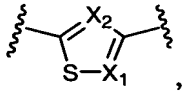
 ,  , -CH=CH(thiophen-2-yl), -CH=CH-unsubstituted phenyl, -$CH_2$(3-NHCOPh-phenyl), -6-bromo-2-(4-ethylphenyl)-4-quinolinyl, -$CH_2$-pyrrolidine, unsubstituted cyclohexyl, unsubstituted benzyl, unsubstituted furan-2-yl, -CH=CH(3-$NO_2$-phenyl), -CH=CH(4-$NO_2$-phenyl), -$CH_2$-naphthyl, unsubstituted naphthyl, unsubstituted thiophene, unsubstituted cyclopropyl, 1,4-benzodioxin, 2-oxo-1-benzopyran, 4-oxo-1-benzopyran, 2-thienyl-quinolin-4-yl, 3-chloro-benzo[b]thiophen-2-yl, 5-Br-(thiophen-2-yl), 5-Cl-(thiophen-2-yl), 5-$NO_2$-(thiophen-2-yl), 5-$NO_2$-(furan-2-yl), 2,5-Cl-(thiophen-3-yl), -CH=CH-(5-$NO_2$-thiophen-2-yl), 5-$NO_2$-(benzothiophen-2-yl), 3-$OCH_3$-(naphth-2-yl), -$CH_2O$(2,4-Cl-phenyl), -$(CH_2)_2S$-phenyl, 2-phenyl-quinolin-4-yl, -$CH_2O$(4-Cl-phenyl), -$CH_2CH_2$-3-(4-Cl-phenyl)-1-phenyl-1-H-pyrazol-4-yl, or –$CH_2$(1,3-dioxoisoindole); and

B) for compounds having the structure:  ,

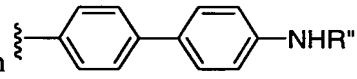
i) when $R^1$ is Cl, and $X_1$ is C-Cl, then $R^3$ is not $NHSO_2$-(2-$CF_3$-phenyl) or –$NHSO_2$-(2,6-dimethoxy-phenyl);

ii) when $R^1$ is $CH_3$, and $X_1$ is C-$CH_3$, then $R^3$ is not an optionally substituted indole or optionally substituted dihydroindole; and

C) for compounds of general formula I, when $Z_1$, $Z_2$ and $Z_3$ are each CH, $R^1$ is H, $X^1$ is CH and $X_2$ is C-$COOCH_3$, then $R^3$ is not 2-(4-ethyl-phenyl)-6-bromo-quinolin-4-yl; and

III. for compounds described above where  is  , one or more of, or all of the following conditions apply:

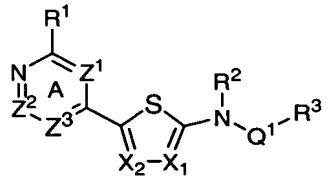
A) when $Z^1$, $Z^2$ and $Z^3$ are each CH, $X^2$ is N, $X^1$ is CH, $Q^1$ is –CONR-, and $R^2$ is hydrogen or -$CH_3$, then $R^3$ is not optionally substituted pyridyl, optionally substituted thiazol-4-yl, -$CH_2$pyridyl, benzimidazol-4-yl, quinolin-2-yl, 1-bromo-isoquinolin-3-yl, benzthiazol-2-yl, optionally substituted 5,6,7,8-tetrahydro-naphthyridin-2-yl, or phenyl substituted with -$CH_2$piperidinyl; and

B) when $Z^1$, $Z^2$ and $Z^3$ are each CH, $X^2$ is N, $X^1$ is CH, $Q^1$ is $SO_2$, and $R^2$ is hydrogen, then $R^3$ is not phenyl substituted with  where R" is hydrogen or -$COCH_3$;

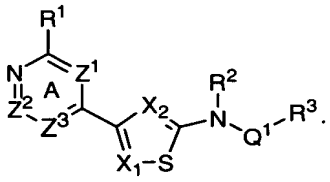
C) when $Z^1$, $Z^2$ and $Z^3$ are each CH, $X_1$ is C-$CO_2H$, $X^2$ is CH, $R^2$ is hydrogen, and $Q^1$ is $SO_2$, then $R^3$ is not 2-$CH_3$-phenyl; and

D) when $Z^1$, $Z^2$ and $Z^3$ are each CH, $X_1$ is CH, $X^2$ is N, $R^2$ is hydrogen, and $Q^1$ is CO, then $R^3$ is not 5-methoxy-6-trifluoromethyl-1H-indole.

2. (Original) The compound of claim 1, wherein the compound has one of the structures:

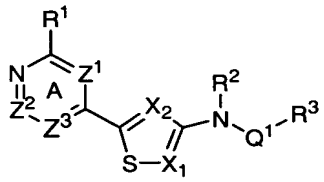


**I-A**



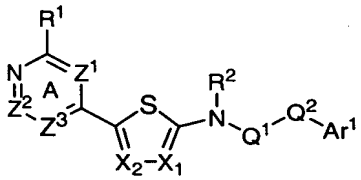
**I-B**

or

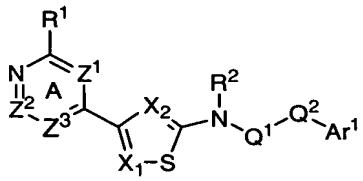


**I-C.**

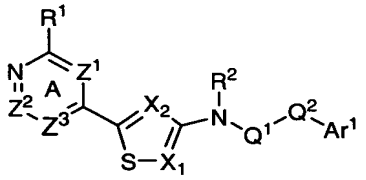
3. (Original) The compound of claim 1, wherein $R^3$ is $Q^2$-$Ar^1$ and compounds have one of formulas **I-A-i, I-B-i,** or **I-C-i**:



**I-A-i**



**I-B-i**



**I-C-i.**

4. (Original) The compound of claim 3, wherein $R^2$ is hydrogen, or is $U_nR'$, where n is 1, and U is a $C_{1-6}$ alkylidene chain wherein one or two methylene units are optionally and independently replaced by O, NR, S, or C(O).

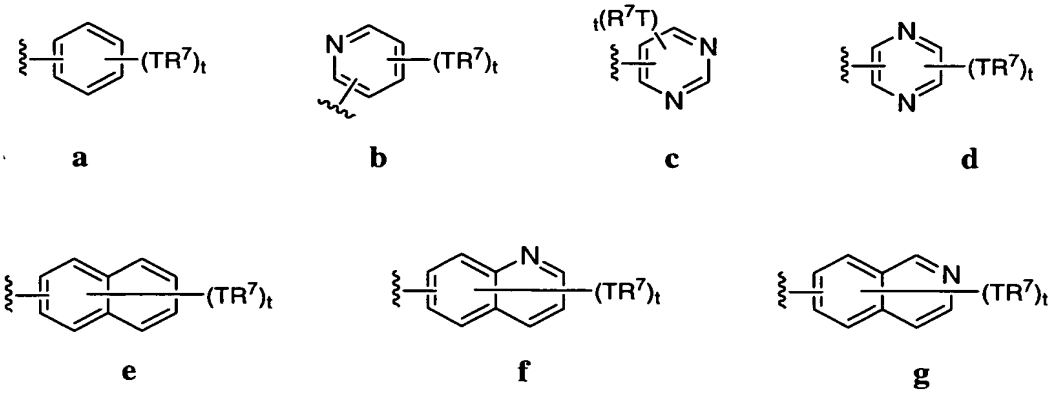
5. (Original) The compound of claim 3, wherein U is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2S-$, $-CH_2NR-$, $-CH_2CH_2O-$, $-CH_2CH_2S-$, $-CH_2CH_2NR-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2NR-$, $-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2CH_2NR-$, $-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or $-CH_2CH_2NHCH_2CH_2-$, and preferred R' groups are hydrogen, $C_1$-$C_4$alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring.

6. (Original) The compound of claim 3, wherein $Q^1$ is –C(O)- or $–SO_2NR$-.

7. (Original) The compound of claim 3, wherein $Q^2$ is a direct bond, or is -$(CHR^6)_q$-, -$(CHR^6)_qO$-, -$(CHR^6)_qS$-, -$(CHR^6)_qS(O)_2$-, -$(CHR^6)_qS(O)$- , -$(CHR^6)_qNR$-, or –$(CHR^6)_qC(O)$-, wherein q is 0, 1, 2, or 3, and $R^6$ is R', -N(R)(R'), -$(CH_2)_{1-4}N(R)(R')$, -OR', -$(CH_2)_{1-4}OR'$, -$NR(CH_2)_{1-4}N(R)(R')$, -$NR(CH_2)_{1-4}SO_2R'$, -$NR(CH_2)_{1-4}COOR'$, or -$NR(CH_2)_{1-4}COR'$, or two occurrences of $R^6$, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring.

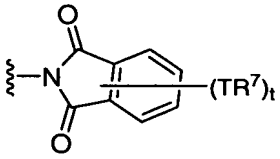
8. (Original) The compound of claim 7, wherein $R^6$ is $CH_2OH$, $CH_2CH_2OH$, OH, OMe, OEt, $NH_2$, NH(Me), NH(Et), N(Me)(Me), $CH_2NH_2$, $CH_2CH_2NH_2$, $NHCO_2t$-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2$pyridyl, $NHSO_2$phenyl, $NHC(O)CH_2C(O)Ot$-butyl, $NHC(O)CH_2NH_3$, and $NHCH_2$-imidazol-4-yl.

9. (Original) The compound of claim 3, wherein $Ar^1$ is:

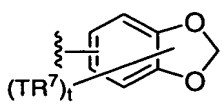



**a** **b** **c** **d**

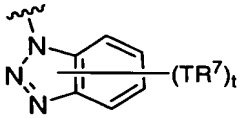
**e** **f** **g**



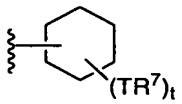
**h**



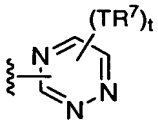
**i**



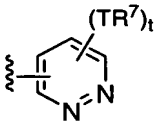
**j**



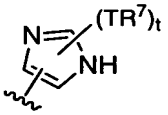
**k**



**l**



**m**



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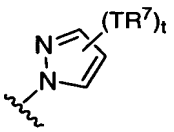

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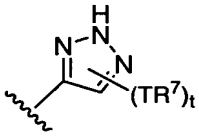
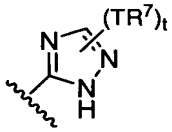
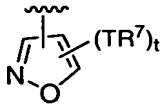


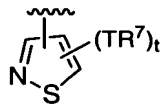
**p**



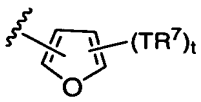
**q**



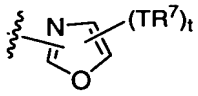
**r**



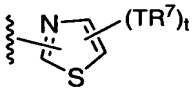
**s**



**t**



**u**



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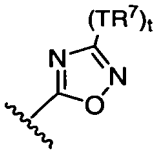
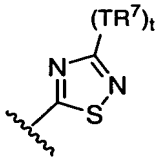
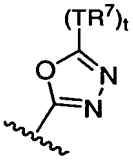


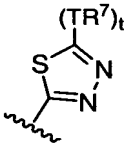
**w**



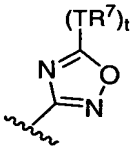
**x**



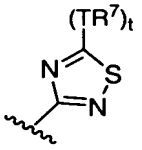
**y**

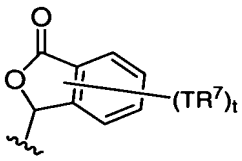


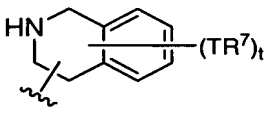
**z**

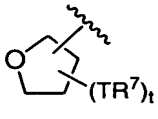


**aa**

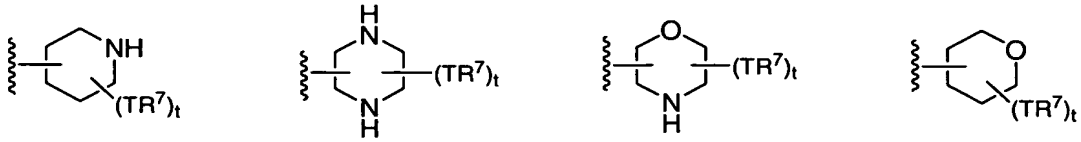




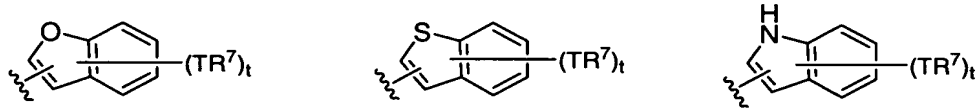




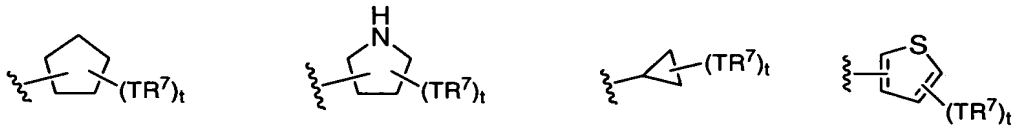
**bb** **cc** **dd** **ee**



**ff** **gg** **hh** **ii**



**jj** **kk** **ll**



**mm** **nn** **oo** **pp**

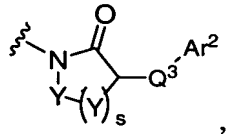
wherein t is 0, 1, 2, 3, 4 or 5, and wherein any $Ar^1$ is bonded to $Q^2$ through any substitutable nitrogen or carbon atom, and wherein one or more hydrogen atoms on any substitutable nitrogen or carbon atom is substituted with one or more independent occurrences of $TR^7$.

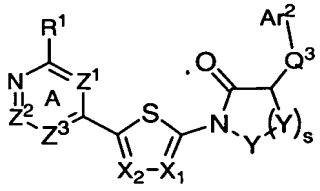
10. (Original) The compound of claim 9, wherein $Ar^1$ is **a, b, e, g, h, i, j, k, r, cc, dd, ff, jj, ll**, or **pp**.

11. (Original) The compound of claim 9, wherein T is a bond or is an optionally substituted $C_{1-6}$ alkylidene chain wherein one or two methylene units are optionally

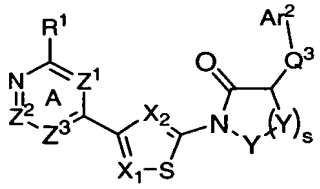
and independently replaced by –O-, -NR-, -S-, -$SO_2$-,–COO-, -CO-, -$OSO_2$-, -$NRSO_2$, -CONR-, or -$SO_2NR$-, and $R^7$ is R' or halogen.

12. (Original) The compound of claim 9, wherein each occurrence of $TR^7$ is independently -$C_{1-3}$alkyl, -OR', -SR', -$CF_3$, -$OCF_3$, -$SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', -$O(CH_2)_4N(R)(R')$, -$O(CH_2)_3N(R)(R')$, -$O(CH_2)_2N(R)(R')$, -$O(CH_2)N(R)(R')$, -$O(CH_2)_4CON(R)(R')$, -$O(CH_2)_3CON(R)(R')$, -$O(CH_2)_2CON(R)(R')$, -$O(CH_2)CON(R)(R')$, -C(O)N(R)(R'), -$(CH_2)_4OR'$, -$(CH_2)_3OR'$, -$(CH_2)_2OR'$, -$CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R'), -$(CH_2)_4N(R)(R')$, -$(CH_2)_3N(R)(R')$, -$(CH_2)_2N(R)(R')$, -$(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, CON(R)(R'), or –$OSO_2R'$.

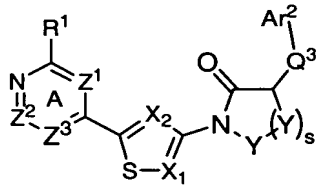
13. (Original) The compound of claim 1, wherein $R^3$ is $Q^2$-$Ar^1$, or $R^2$ and $Q^1$-$R^3$, taken together with the nitrogen atom, form the cyclic group:  , where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -$SO_2$-, -O-, -S-, -$NR^5$-, or -$C(R^5)_2$-, and $R^5$ is $U_nR'$, and compounds of formula **I-A-ii, I-B-ii,** and **I-C-ii** are provided:



**I-A-ii**



**I-B-ii**



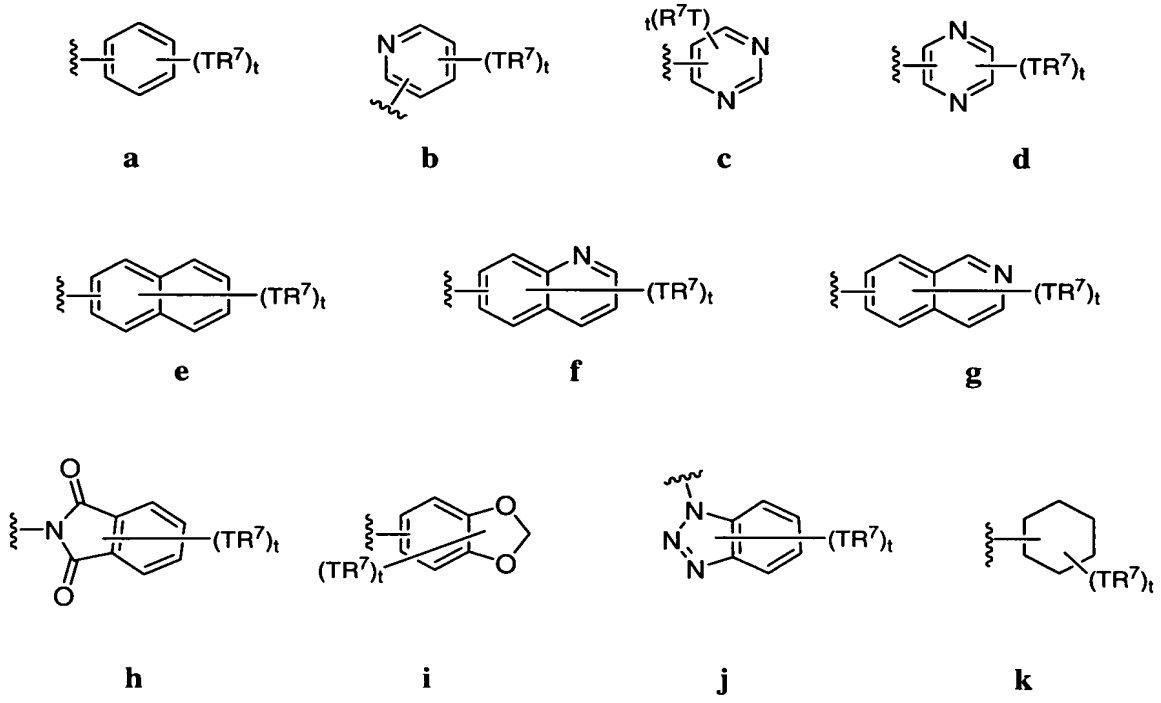
**I-C-ii.**

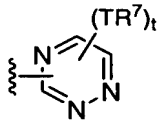
14. (Original) The compound of claim 13, wherein $Q^3$ is a direct bond, or is -$(CHR^6)_q$-, -$(CHR^6)_qO$-, -$(CHR^6)_qS$-, -$(CHR^6)_qS(O)_2$-, -$(CHR^6)_qS(O)$- , -$(CHR^6)_qNR$-, or –$(CHR^6)_qC(O)$-, wherein q is 0, 1, 2, or 3, and $R^6$ is R', -N(R)(R'), -$(CH_2)_1$-.

$_4$N(R)(R'), -OR', -$(CH_2)_{1-4}$OR', -NR$(CH_2)_{1-4}$N(R)(R'), -NR$(CH_2)_{1-4}SO_2$R', -NR$(CH_2)_{1-4}$COOR', or -NR$(CH_2)_{1-4}$COR', or two occurrences of $R^6$, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring.

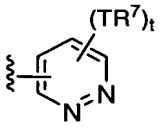
15. (Original) The compound of claim 14, wherein $R^6$ is $CH_2OH$, $CH_2CH_2OH$, OH, OMe, OEt, $NH_2$, NH(Me), NH(Et), N(Me)(Me), $CH_2NH_2$, $CH_2CH_2NH_2$, $NHCO_2t$-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2$pyridyl, $NHSO_2$phenyl, $NHC(O)CH_2C(O)Ot$-butyl, $NHC(O)CH_2NH_3$, and $NHCH_2$-imidazol-4-yl.

16. (Original) The compound of claim 13, wherein $Ar^2$ is:

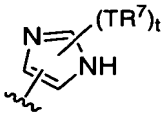




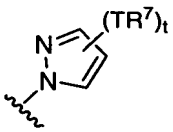
**l**



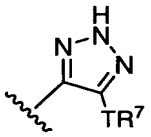
**m**



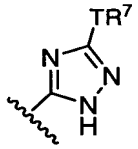
**n**



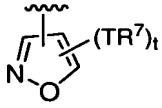
**o**



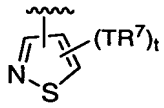
**p**



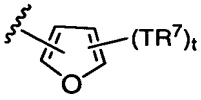
**q**



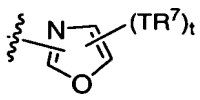
**r**



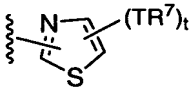
**s**



**t**



**u**



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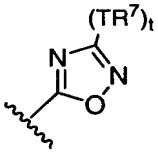
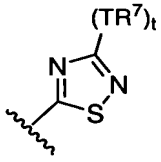
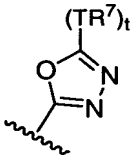


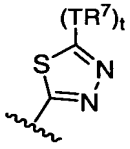
**w**



**x**



**y**



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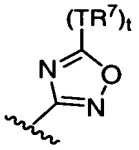

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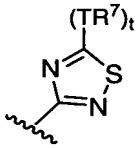

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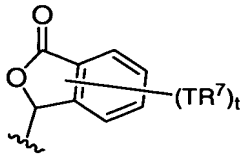
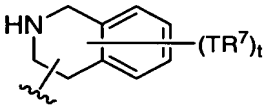


**cc**



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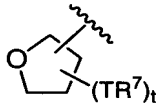

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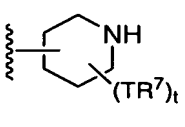

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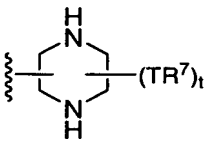

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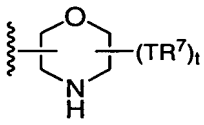

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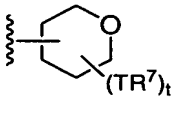

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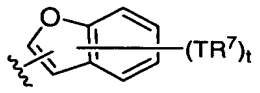


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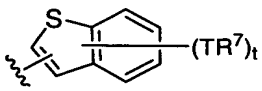


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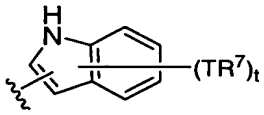


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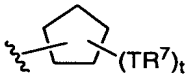


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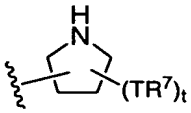


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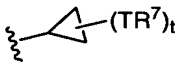


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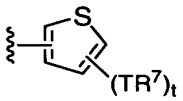



**pp**

wherein t is 0, 1, 2, 3, 4 or 5, and wherein any $Ar^2$ is bonded to $Q^3$ through any substitutable nitrogen or carbon atom, and wherein one or more hydrogen atoms on any substitutable nitrogen or carbon atom is substituted with one or more independent occurrences of $TR^7$.

17. (Original) The compound of claim 16, wherein $Ar^2$ is **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**.

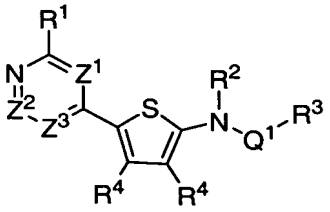
18. (Original) The compound of claim 16, wherein T is a bond or is an optionally substituted $C_{1-6}$ alkylidene chain wherein one or two methylene units are optionally and independently replaced by –O-, -NR-, -S-, $-SO_2-$,–COO-, -CO-, $-OSO_2-$, $-NRSO_2$, -CONR-, or $-SO_2NR-$, and $R^7$ is R' or halogen.

19. (Original) The compound of claim 16, wherein each occurrence of $TR^7$ is independently $-C_{1-3}$alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$,

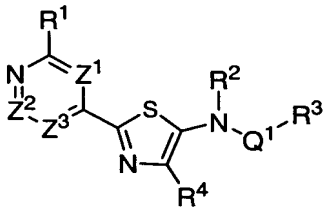
-O($CH_2$)CON(R)(R'), -C(O)N(R)(R'), -($CH_2$)$_4$OR', -($CH_2$)$_3$OR', -($CH_2$)$_2$OR', -$CH_2$OR', optionally substituted phenyl or benzyl, -N(R)(R'), -($CH_2$)$_4$N(R)(R'), -($CH_2$)$_3$N(R)(R'), -($CH_2$)$_2$N(R)(R'), -($CH_2$)N(R)(R'), or $SO_2$N(R)(R'), N$RSO_2$R', CON(R)(R'), or –O$SO_2$R'.

20. (Original) The compound of claim 13, wherein $R^5$ is hydrogen, ($CH_2$)$_3$OR', ($CH_2$)$_2$OR', ($CH_2$)OR', ($CH_2$)$_3$N(R')$_2$, ($CH_2$)$_2$N(R')$_2$, ($CH_2$)N(R')$_2$, or $C_{1-4}$aliphatic.

21. (Original) The compound of claim 1, wherein $X^1$ and $X^2$ are each independently $CR^4$ or N, and compounds have one of formulas **II, III, IV, V, VI, VII, VIII, IX, X, XI, XII,** or **XIII**:



**II**



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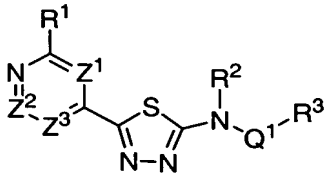

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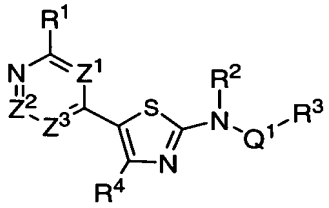
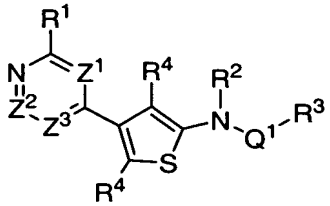


**V**



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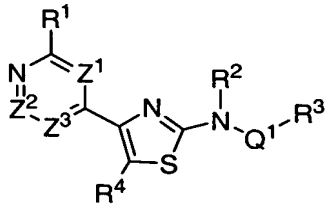
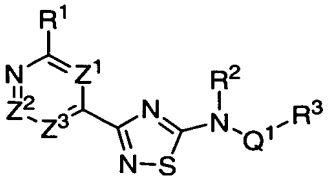
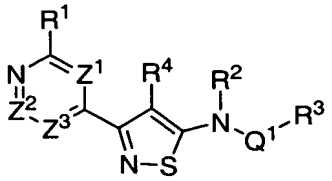


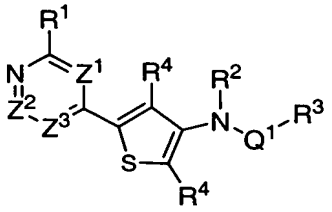
**VII**



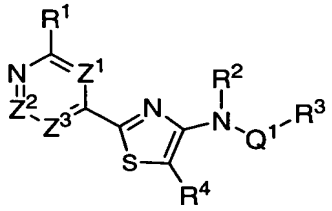
VIII



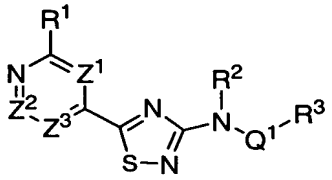
IX



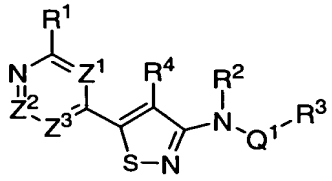
X



XI

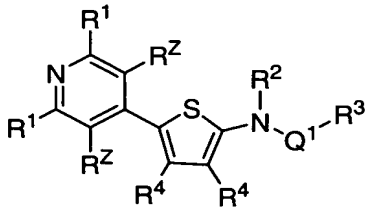


XII

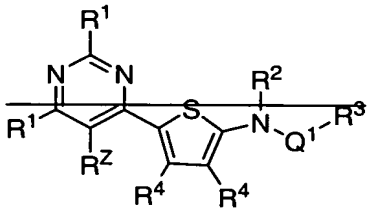


XIII

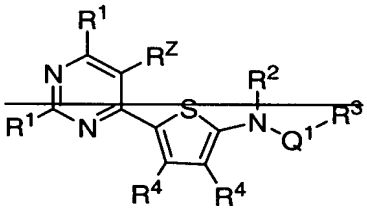
22. (Currently amended) The compound of claim 21, wherein compounds have one of formulas **II-A**, ~~**II-B, II-C, II-D, II-E, II-F,**~~ **III-A**, ~~**III-B, III-C, III-D, III-E, III-F,**~~ **IV-A**, ~~**IV-B, IV-C, IV-D, IV-E, IV-F,**~~ **V-A**, ~~**V-B, V-C, V-D, V-E, V-F,**~~ **VI-A**, ~~**VI-B, VI-C, VI-D, VI-E, VI-F,**~~ **VII-A**, ~~**VII-B, VII-C, VII-D, VII-E, VII-F,**~~ **VIII-A**, ~~**VIII-B, VIII-C, VIII-D, VIII-E, VIII-F,**~~ **IX-A**, ~~**IX-B, IX-C, IX-D, IX-E, IX-F,**~~ **X-A**, ~~**X-B, X-C, X-D, X-E, X-F,**~~ **XI-A**, ~~**XI-B, XI-C, XI-D, XI-E, XI-F,**~~ **XII-A**, ~~**XII-B, XII-C, XII-D, XII-E, XII-F,**~~ or **XIII-A**, ~~**XIII-B, XIII-C, XIII-D, XIII-E, or XIII-F**~~:



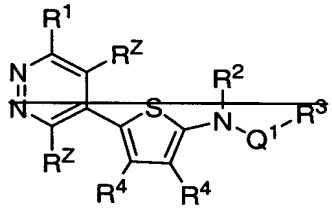
II-A



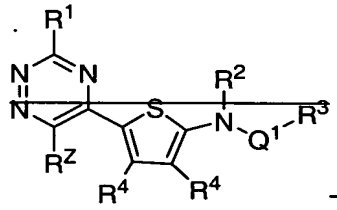
~~II-B~~



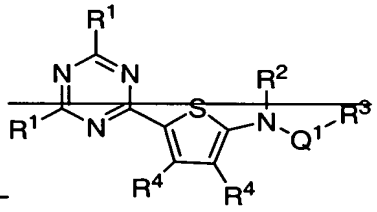
~~II-C~~



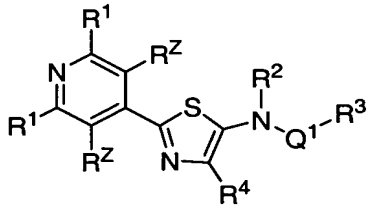
~~II-D~~



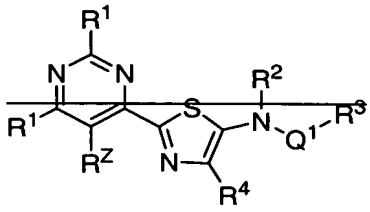
~~II-E~~



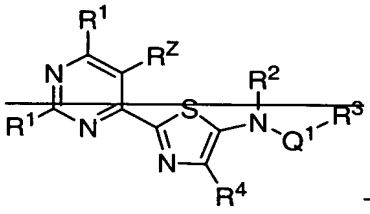
~~II-F~~



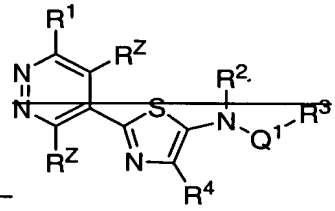
III-A



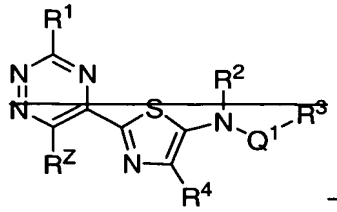
~~III-B~~



~~III-C~~



~~III-D~~



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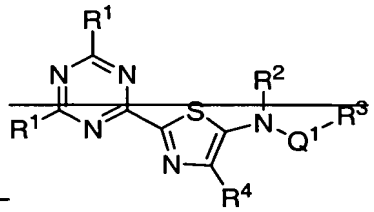
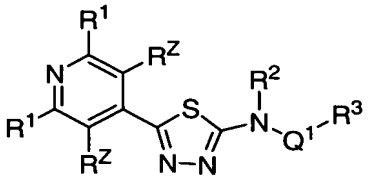
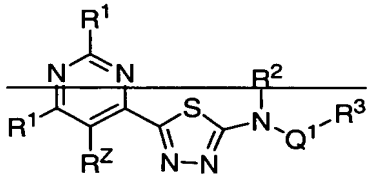


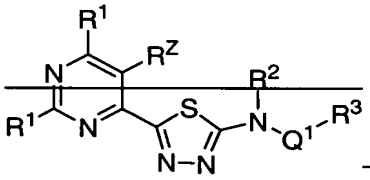
~~III-F~~



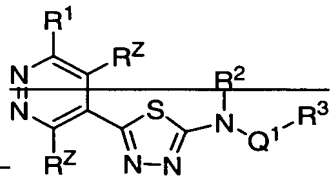
IV-A



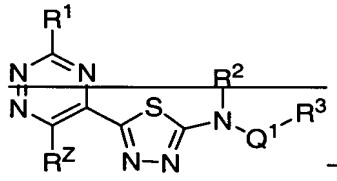
~~IV-B~~



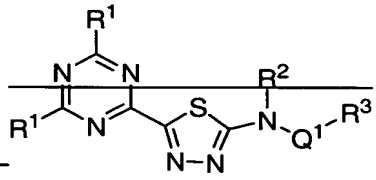
~~IV-C~~



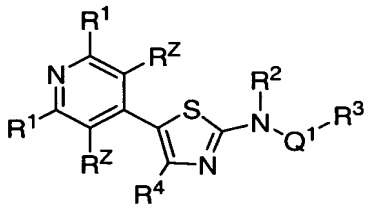
~~IV-D~~



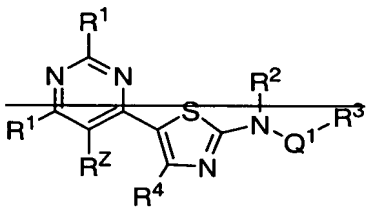
~~IV-E~~



~~IV-F~~



V-A



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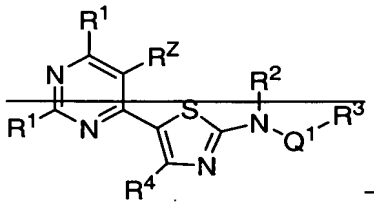
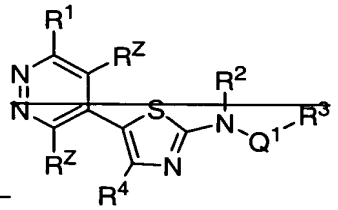
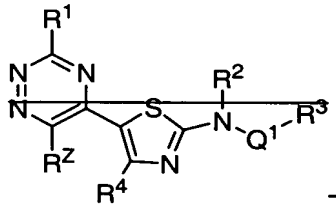
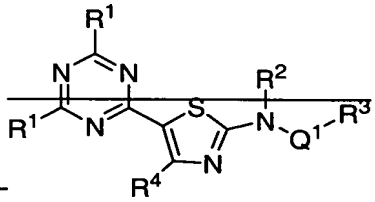




~~V-C~~ ~~V-D~~





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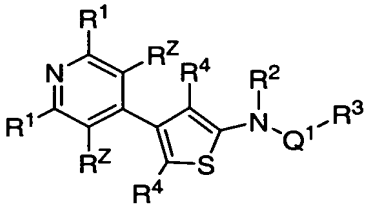
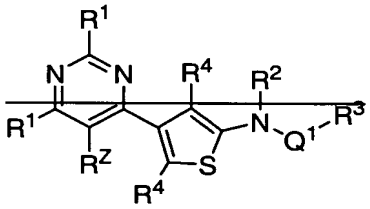


VI-A



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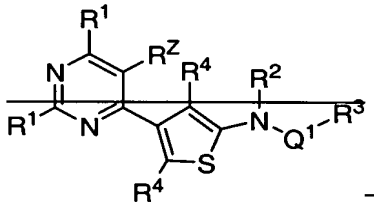

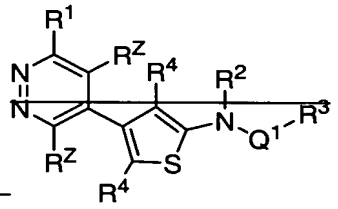

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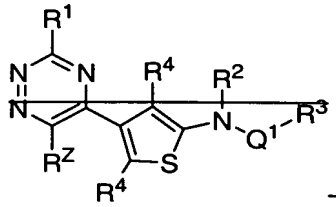

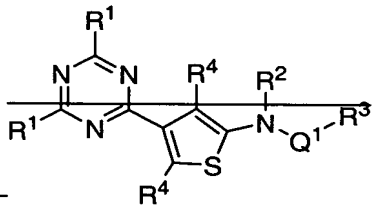

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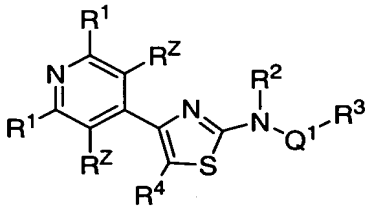
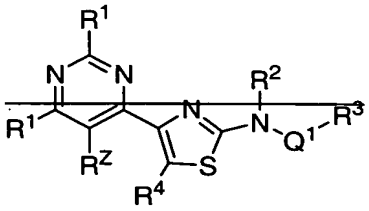


VII-A



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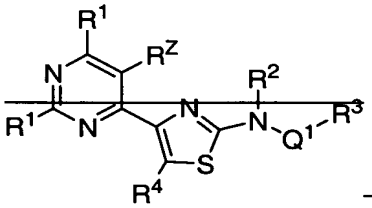

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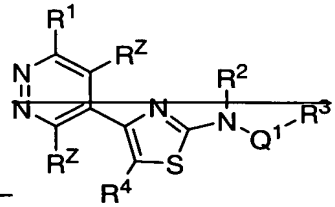

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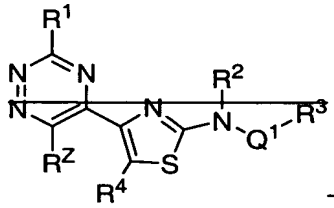

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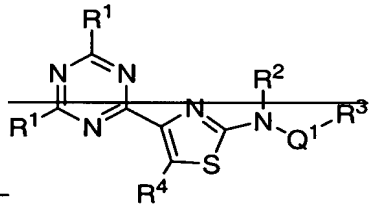

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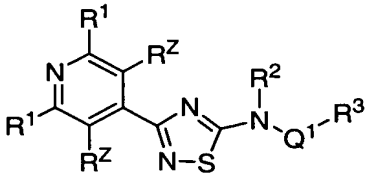
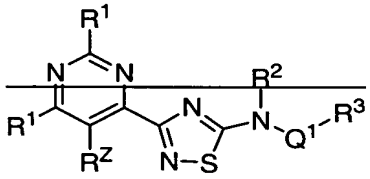


VIII-A



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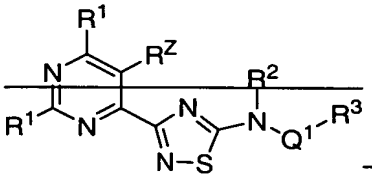

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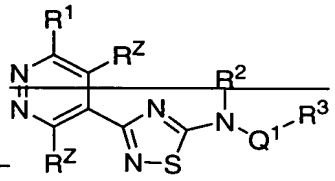

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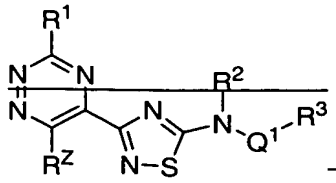

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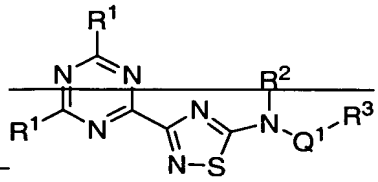

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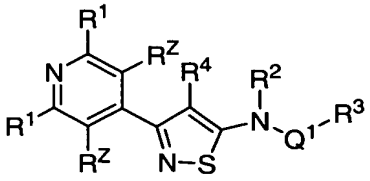
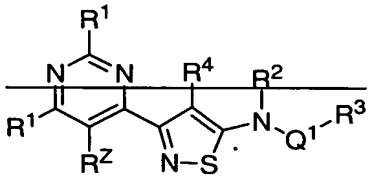


**IX-A**



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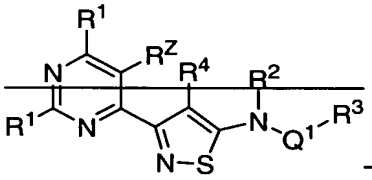

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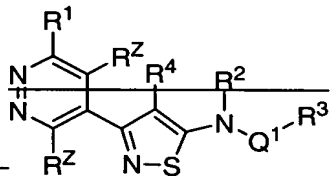

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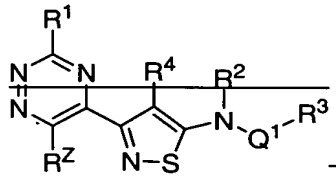

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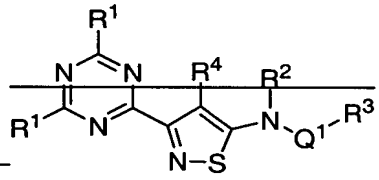

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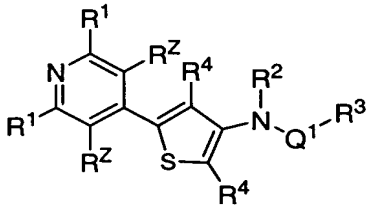

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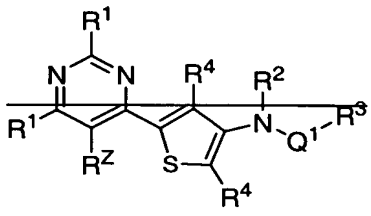

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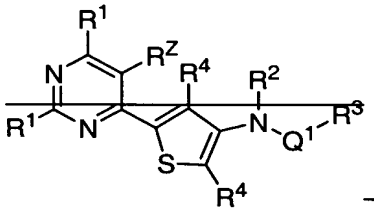

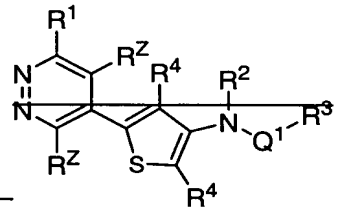

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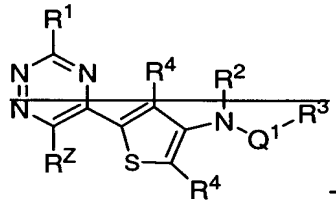

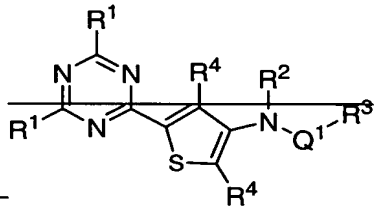

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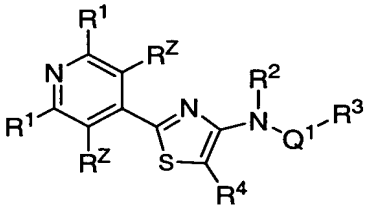
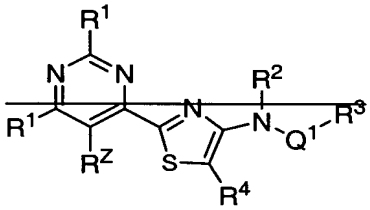


XI-A



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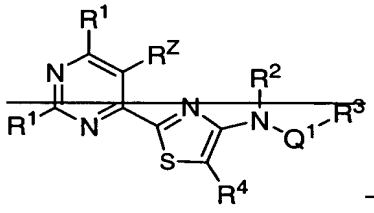

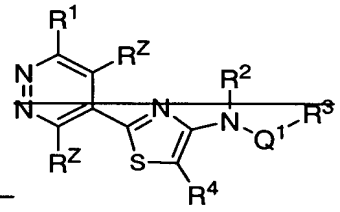

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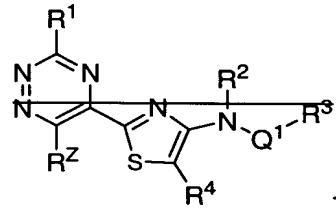

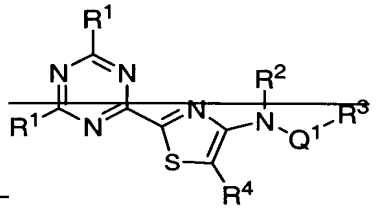

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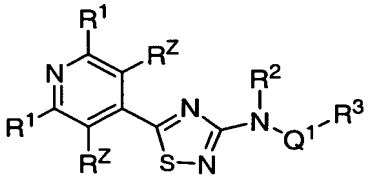
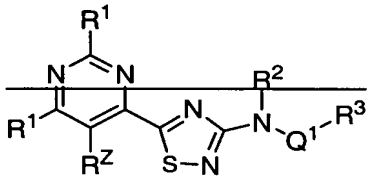


**XII-A**



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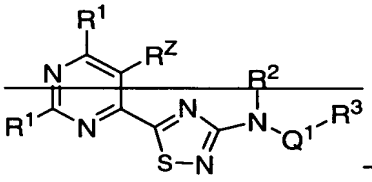

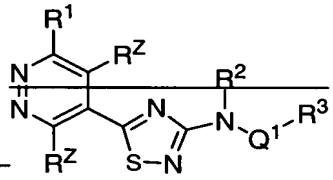

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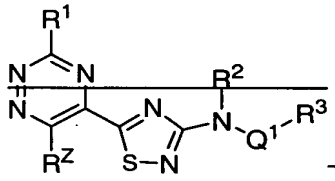

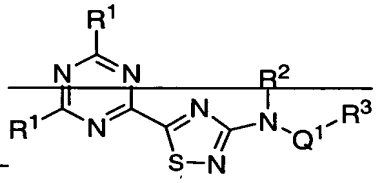

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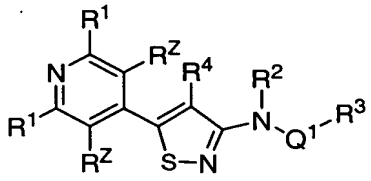
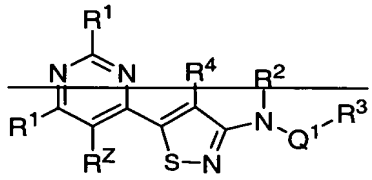


**XIII-A**



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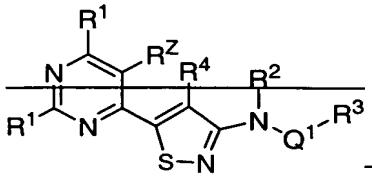

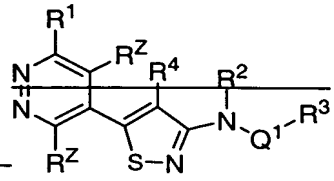

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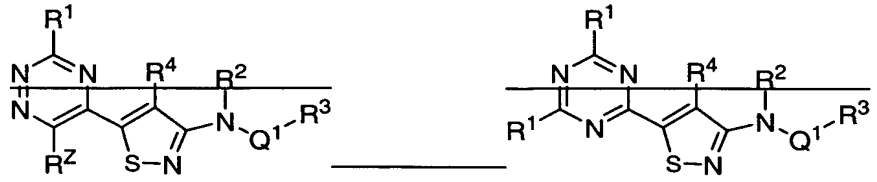


~~XIII-E~~ ~~XIII-F~~

23. (Original) The compound of claim 1, wherein each occurrence of $R^1$ is independently hydrogen, halogen, optionally substituted $C_1$-$C_4$aliphatic, OR, SR, or $N(R)_2$.

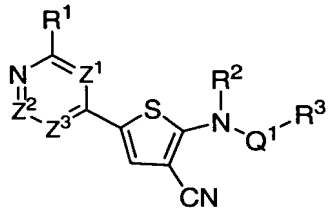
24. (Original) The compound of claim 23, wherein each occurrence of $R^1$ is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, -OH, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $NH(CH_2)_2NHCH_3$, NH(cyclopropyl), $NH(CH_2)$cyclopropyl, or $NH(CH_2)_2N(CH_3)_2$.

25. (Original) The compound of claim 1, wherein each occurrence of $R^Z$ is independently hydrogen, halogen, $C_1$-$C_4$aliphatic, OH, OR', or N(R)(R').

26. (Original) The compound of claim 25, wherein each occurrence of $R^Z$ is independently hydrogen, halogen, Me, OH, OMe, $NH_2$, or $N(Me)_2$.

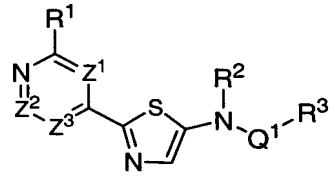
27. (Original) The compound of claim 1, wherein $R^4$ groups are each independently hydrogen, $C_{1-6}$aliphatic, CN, COR, C(=O)OR, $C(=O)N(R)_2$, or halogen.

28. (Original) The compound of claim 1, wherein one occurrence of $R^4$ is CN and compounds have the general structure **II-a**:



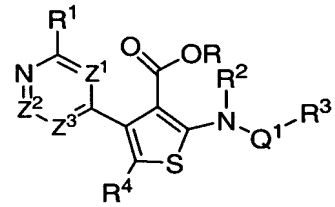
**II-a**

29. (Original) The compound of claim 1, wherein $R^4$ is hydrogen and compounds have the general structure **III-a**:



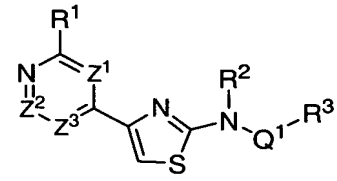
**III-a**

30. (Original) The compound of claim 1, wherein one occurrence of $R^4$ is hydrogen and the other occurrence of $R^4$ is -COOR and compounds have the general structure **VI-a**:



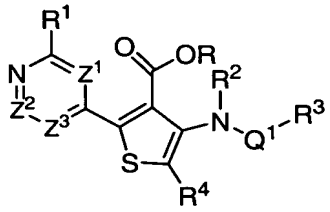
**VI-a**

31. (Original) The compound of claim 1, wherein $R^4$ is hydrogen and compounds have the general structure **VII-a**:



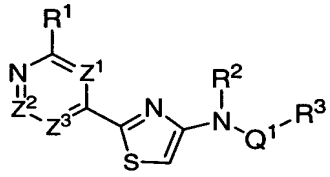
**VII-a**

32. (Original) The compound of claim 1, wherein one occurrence of $R^4$ is hydrogen and the other occurrence of $R^4$ is C(=O)OR and compounds have the general structure **X-a**:



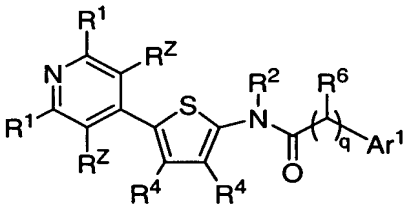
**X-a**

33. (Original) The compound of claim 1, wherein $R^4$ is hydrogen and compounds have the general structure **XI-a**:

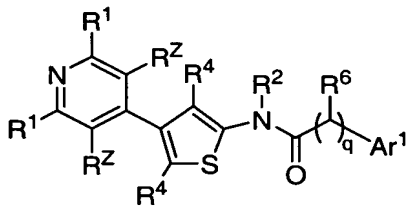


**XI-a**

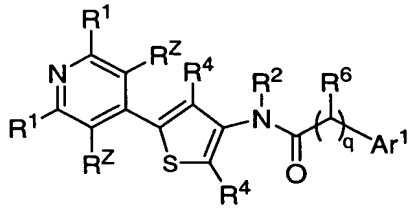
34. (Original) The compound of claim 1, wherein $Q^1$ is -CO-, $Q^2$ is $CHR^6$, q is 1 2, or 3, and compounds have one of formulas **XIV, XV,** or **XVI:**



**XIV**

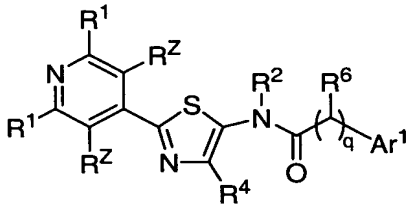


**XV**

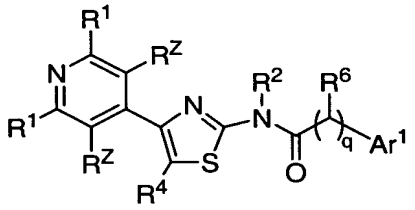


**XVI**

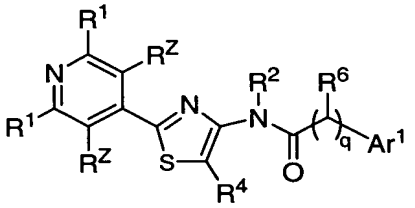
35. (Original) The compound of claim 1, wherein $Q^1$ is -CO-, $Q^2$ is $CHR^6$, q is 1, 2 or 3, and compounds have one of formulas **XVII, XVIII,** or **XIX:**



**XVII**



**XVIII**



**XIX**

36. (Original) The compound of claims 34 or 35, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of $R^1$ is independently hydrogen, halogen, optionally substituted $C_1$-$C_4$aliphatic, OR, SR, or $N(R)_2$;

b) each occurrence of $R^1$ is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, -OH, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $NH(CH_2)_2NHCH_3$, NH(cyclopropyl), $NH(CH_2)$cyclopropyl, or $NH(CH_2)_2N(CH_3)_2$;

c) each occurrence of $R^Z$ is independently hydrogen, halogen, optionally substituted $C_1$-$C_4$aliphatic, OH, O(R'), or N(R)(R');

d) each occurrence of $R^Z$ is independently hydrogen, halogen, Me, OH, OMe, $NH_2$, or $N(Me)_2$;

e) $R^2$ is hydrogen, or is $U_nR'$, where n is 1, and U is–$CH_2$-, -$CH_2CH_2$-, –$CH_2CH_2CH_2$-, -$CH_2CH_2CH_2CH_2$-, -$CH_2O$-, -$CH_2S$-, –$CH_2NR$-, -$CH_2CH_2O$-, -$CH_2CH_2S$-, –$CH_2CH_2NR$-, -$CH_2CH_2CH_2O$-, -$CH_2CH_2CH_2S$-, -$CH_2CH_2CH_2NR$-, -$CH_2CH_2CH_2CH_2O$-, -$CH_2CH_2CH_2CH_2S$-, -$CH_2CH_2CH_2CH_2NR$-, -$CH_2CH_2OCH_2CH_2$-, -$(CH_2)_4NHCH_2$-, -$(CH_2)_3NHCH_2CH_2$-, or -$CH_2CH_2NHCH_2CH_2$-, and R' groups are hydrogen, $C_1$-$C_4$alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;

f) each occurrence of $R^4$ is independently hydrogen, $C_{1-6}$aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

g) q is 1, 2, or 3;

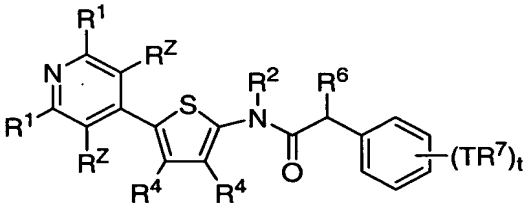
h) $R^6$ is R', -N(R)(R'), -$(CH_2)_{1-4}$N(R)(R'), -OR', -$(CH_2)_{1-4}$OR', -NR$(CH_2)_{1-4}$N(R)(R'), -NR$(CH_2)_{1-4}SO_2$R', -NR$(CH_2)_{1-4}$COOR', or -NR$(CH_2)_{1-4}$COR', or two occurrences of $R^6$, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring;

i) $R^6$ is $CH_2OH$, $CH_2CH_2OH$, OH, OMe, OEt, $NH_2$, NH(Me), NH(Et), N(Me)(Me), $CH_2NH_2$, $CH_2CH_2NH_2$, $NHCO_2$*t*-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2$pyridyl, $NHSO_2$phenyl, $NHC(O)CH_2C(O)O$*t*-butyl, $NHC(O)CH_2NH_3$, and $NHCH_2$-imidazol-4-yl;

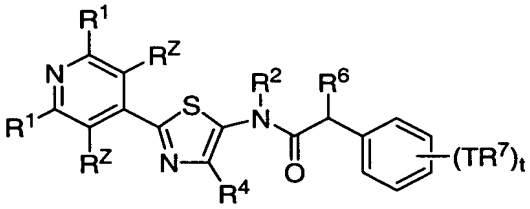
j) $Ar^1$ is ring **a, b, e, g, h, i, j, k, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted $C_{1-6}$ alkylidene chain wherein one or two methylene units are optionally and independently replaced by –O-, -NR-, -S-, -$SO_2$-,–COO-, -CO-, -$OSO_2$-, -$NRSO_2$, -CONR-, or -$SO_2$NR-, and $R^7$ is R' or halogen; or

k) $Ar^1$ is ring **a, b, e, g, h, i, j, k, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and each occurrence of $TR^7$ is independently -$C_{1-3}$alkyl, -OR', -SR', -$CF_3$, -$OCF_3$, -$SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', -$O(CH_2)_4N(R)(R')$, -$O(CH_2)_3N(R)(R')$, -$O(CH_2)_2N(R)(R')$, -$O(CH_2)N(R)(R')$, -$O(CH_2)_4CON(R)(R')$, -$O(CH_2)_3CON(R)(R')$, -$O(CH_2)_2CON(R)(R')$, -$O(CH_2)CON(R)(R')$, -$C(O)N(R)(R')$, -$(CH_2)_4OR'$, -$(CH_2)_3OR'$, -$(CH_2)_2OR'$, -$CH_2OR'$, optionally substituted phenyl or benzyl, -$N(R)(R')$, -$(CH_2)_4N(R)(R')$, -$(CH_2)_3N(R)(R')$, -$(CH_2)_2N(R)(R')$, -$(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, $CON(R)(R')$, or $-OSO_2R'$.

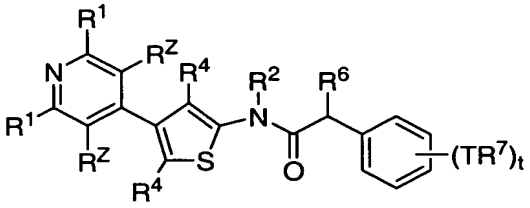
37. (Original) The compound of claim 34 or 35, q is 1, and $Ar^1$ is optionally substituted phenyl and compounds of general formula **XIV-A** through **XIX-A** are provided:



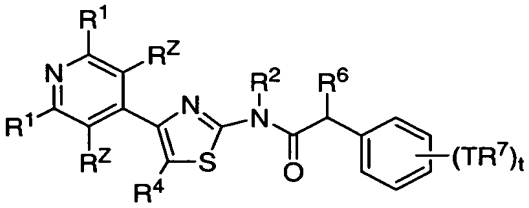
**XIV-A**



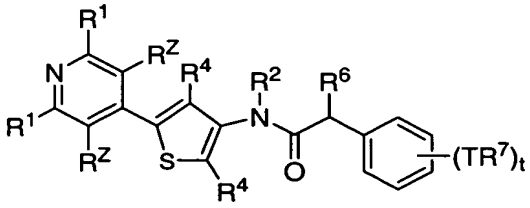
**XV-A**



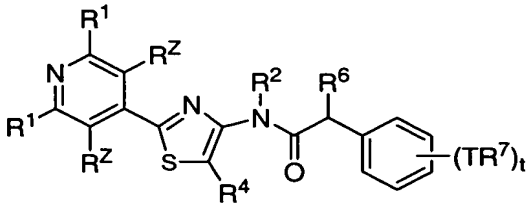
**XVI-A**



**XVII-A**



**XVIII-A**



**XIX-A**

wherein:

each occurrence of $R^1$ is hydrogen;

each occurrence of $R^Z$ is hydrogen;

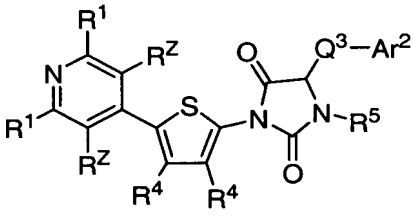
$R^2$ is hydrogen, or is $U_nR'$, where n is 1, and U is–$CH_2$-, -$CH_2CH_2$-, –$CH_2CH_2CH_2$-, -$CH_2CH_2CH_2CH_2$-, -$CH_2O$-, -$CH_2S$-, –$CH_2NR$-, -$CH_2CH_2O$-, -$CH_2CH_2S$-, –$CH_2CH_2NR$-, -$CH_2CH_2CH_2O$-, -$CH_2CH_2CH_2S$-, -$CH_2CH_2CH_2NR$-, -$CH_2CH_2CH_2CH_2O$-, -$CH_2CH_2CH_2CH_2S$-, -$CH_2CH_2CH_2CH_2NR$-, -$CH_2CH_2OCH_2CH_2$-, -$(CH_2)_4NHCH_2$-, -$(CH_2)_3NHCH_2CH_2$-, or -$CH_2CH_2NHCH_2CH_2$-, and R' groups are hydrogen, $C_1$-$C_4$alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;

each occurrence of $R^4$ is independently hydrogen, $C_{1-6}$aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

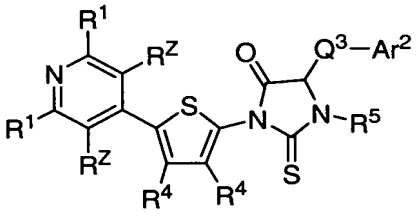
$R^6$ is R', -N(R)(R'), -$(CH_2)_{1-4}$N(R)(R'), -OR', -$(CH_2)_{1-4}$OR', -$NR(CH_2)_{1-4}$N(R)(R'), -$NR(CH_2)_{1-4}SO_2$R', -$NR(CH_2)_{1-4}$COOR', or -$NR(CH_2)_{1-4}$COR'; and

t is 0, 1, 2, or 3, and each occurrence of $TR^7$ is independently -$C_{1-3}$alkyl, -OR', -SR', -$CF_3$, -$OCF_3$, -$SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', -$O(CH_2)_4N(R)(R')$, -$O(CH_2)_3N(R)(R')$, -$O(CH_2)_2N(R)(R')$, -$O(CH_2)N(R)(R')$, -$O(CH_2)_4CON(R)(R')$, -$O(CH_2)_3CON(R)(R')$, -$O(CH_2)_2CON(R)(R')$, -$O(CH_2)CON(R)(R')$, -C(O)N(R)(R'), -$(CH_2)_4OR'$, -$(CH_2)_3OR'$, -$(CH_2)_2OR'$, -$CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R'), -$(CH_2)_4N(R)(R')$, -$(CH_2)_3N(R)(R')$, -$(CH_2)_2N(R)(R')$, -$(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, CON(R)(R'), or –$OSO_2R'$.

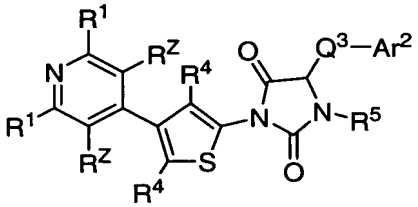
38. (Original) The compound of claim 1, wherein $R^2$ and $Q^1$-$R^3$, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula **XX** through **XXV:**



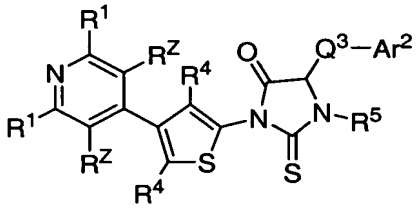
**XX**



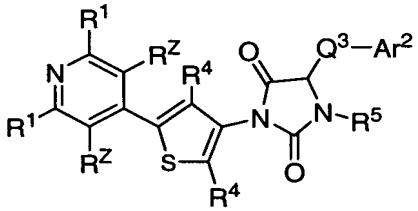
**XXI**



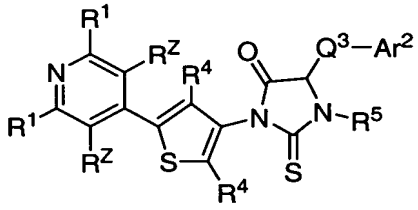
**XXII**



**XXIII**

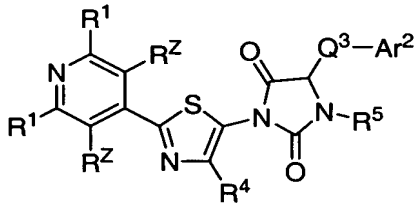


**XXIV**

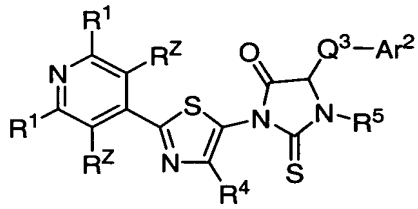


**XXV**

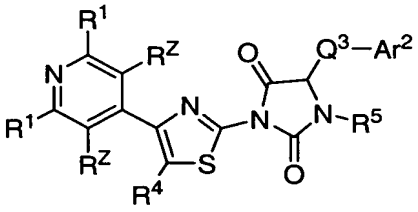
39. (Original) The compound of claim 1, $R^2$ and $Q^1$-$R^3$, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula **XXVI** through **XXXI:**



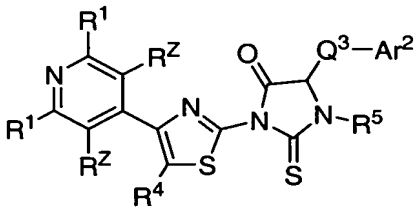
**XXVI**



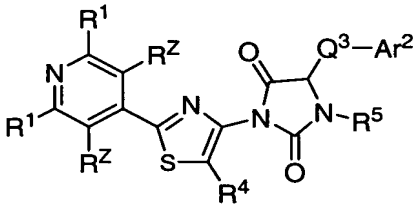
**XXVII**



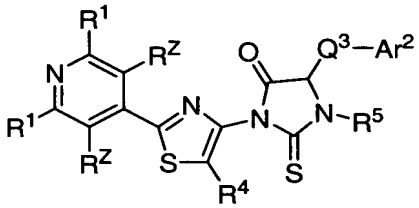
**XXVIII**



**XXIX**

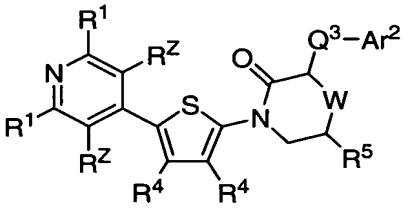


**XXX**

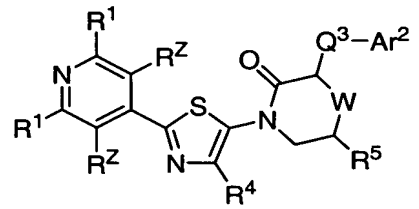


**XXXI**

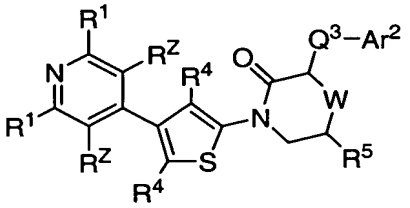
40. (Original) The compound of claim 1, wherein $R^2$ and $Q^1$-$R^3$, taken together with the atoms to which they are bound form a 6-membered cyclic group, and compounds have the general formula **XXXII** through **XXXVII:**



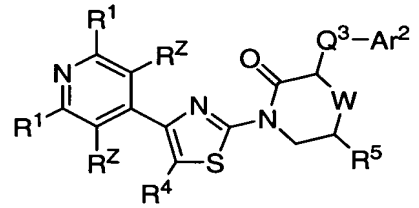
**XXXII**



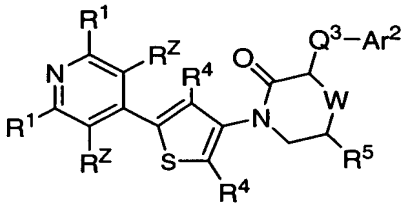
**XXXIII**

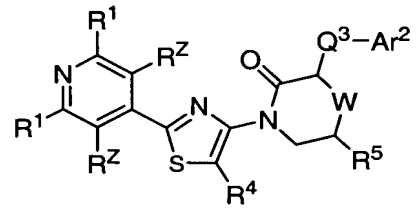


**XXXIV**



**XXXV**





**XXXVI** **XXXVII**

wherein W is O, $NR^5$, or $CHR^5$.

41. (Original) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of $R^1$ is independently hydrogen, halogen, optionally substituted $C_1$-$C_4$aliphatic, OR, SR, or $N(R)_2$;

b) each occurrence of $R^Z$ is independently hydrogen, halogen, optionally substituted $C_1$-$C_4$aliphatic, OH, OR' or N(R)(R');

c) each occurrence of $R^4$ is independently hydrogen, $C_{1-6}$aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

d) $R^5$ is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or $C_{1-4}$aliphatic;

e) $Q^3$ is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$ , $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

f) $Ar^2$ is ring **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted $C_{1-6}$ alkylidene chain wherein one or two methylene units are optionally and independently replaced by –O-, -NR-, -S-, $-SO_2-$,–COO-, -CO-, $-OSO_2-$, $-NRSO_2$, -CONR-, or $-SO_2NR-$, and $R^7$ is R' or halogen.

42. (Original) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of $R^1$ is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, -OH, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $NH(CH_2)_2NHCH_3$, NH(cyclopropyl), $NH(CH_2)$cyclopropyl, or $NH(CH_2)_2N(CH_3)_2$;

b) each occurrence of $R^Z$ is independently hydrogen, halogen, Me, OH, OMe, $NH_2$, or $N(Me)_2$;

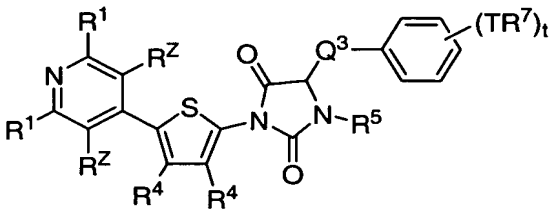
c) each occurrence of $R^4$ is independently hydrogen, $C_{1-6}$aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

d) $R^5$ is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or $C_{1-4}$aliphatic;

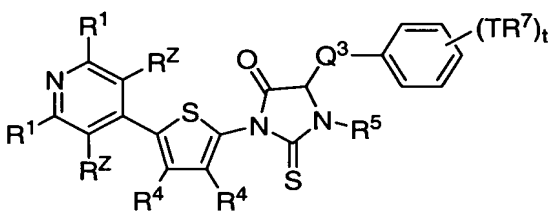
e) $Q^3$ is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$ , $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

f) $Ar^2$ is ring **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and each occurrence of $TR^7$ is independently $-C_{1-3}$alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, $-C(O)N(R)(R')$, $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, $-N(R)(R')$, $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, $CON(R)(R')$, or $-OSO_2R'$.

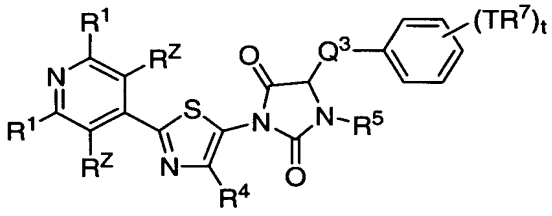
43. (Original) The compound of claims 38, 39 or 40, wherein $Ar^2$ is optionally substituted phenyl and compounds of general formula **XX-A**, through **XXXVII** are provided:



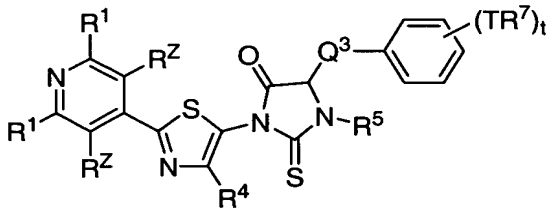
**XX-A**



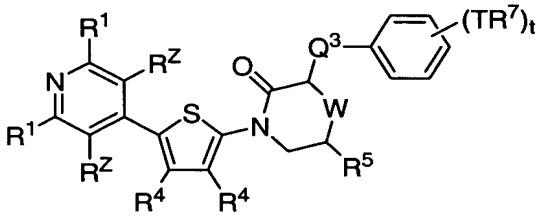
**XXI-A**



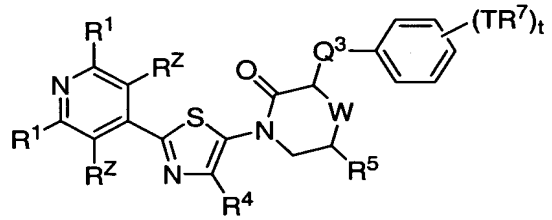
**XXII-A**



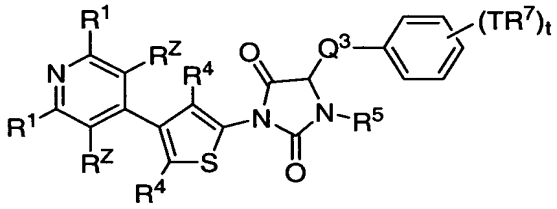
**XXIII-A**



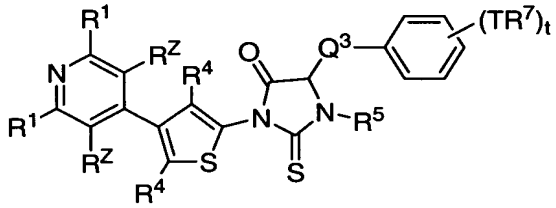
**XXIV-A**



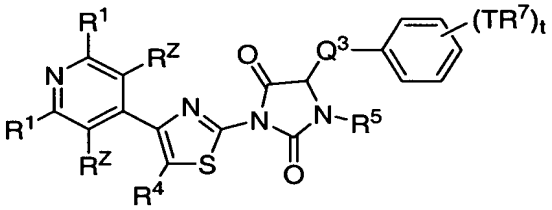
**XXV-A**



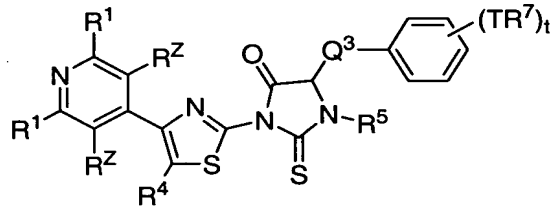
**XXVI-A**



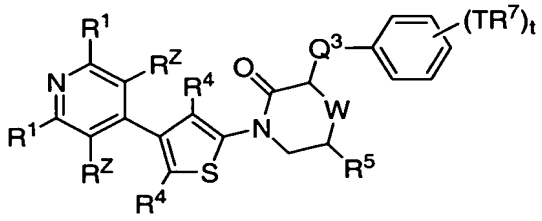
**XXVII-A**



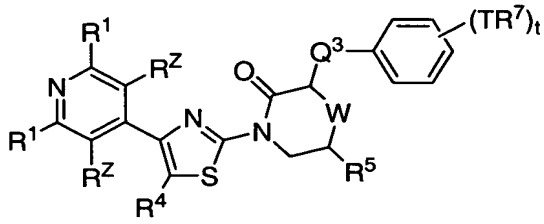
**XXVIII-A**



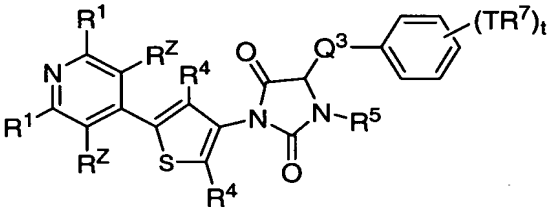
**XXIX-A**



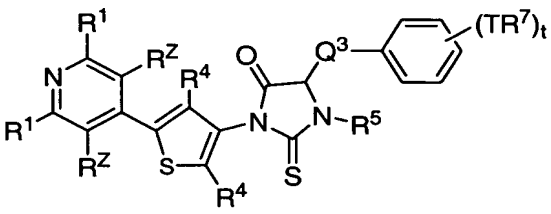
**XXX-A**



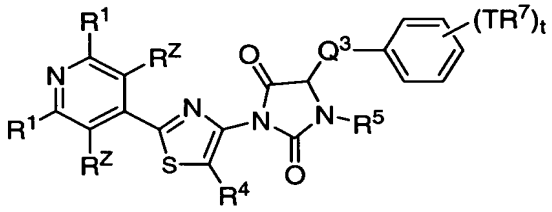
**XXXI-A**



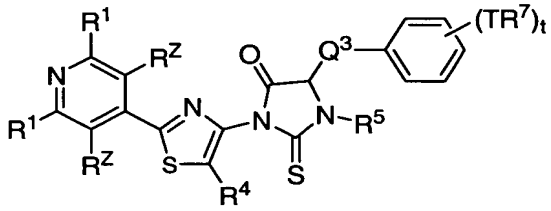
**XXXII-A**



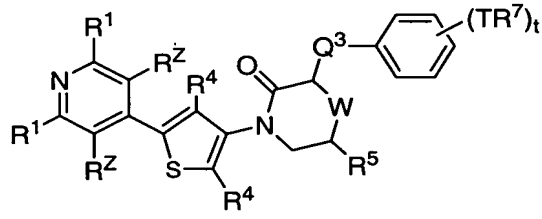
**XXXIII-A**



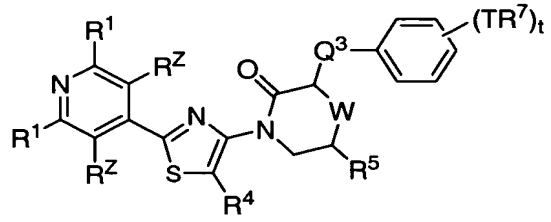
**XXXIV-A**



**XXXV-A**



**XXXVI-A**



**XXXVII-A**

44. (Original) The compound of claim 43, wherein compound variables are selected from:

each occurrence of $R^1$ is hydrogen;

each occurrence of $R^Z$ is hydrogen;

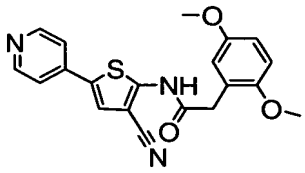
each occurrence of $R^4$ is independently hydrogen, $C_{1-6}$aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

$R^5$ is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or $C_{1-4}$aliphatic;

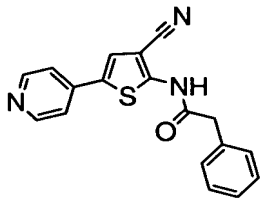
$Q^3$ is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$ , $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

t is 0, 1, 2, or 3, and each occurrence of $TR^7$ is independently $-C_{1-3}$alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, $-C(O)N(R)(R')$, $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, $-N(R)(R')$, $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, $CON(R)(R')$, or $-OSO_2R'$.

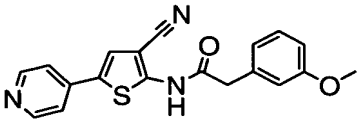
45. (Currently amended) The compound of claim 1, having one of the structures:



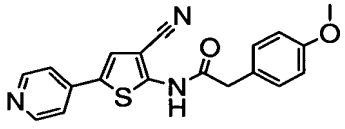
**I-A-1**



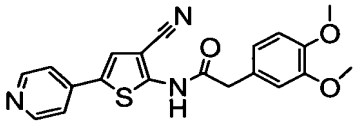
**I-A-2**



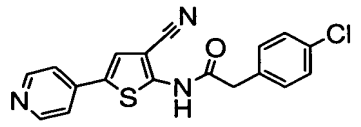
**I-A-3**



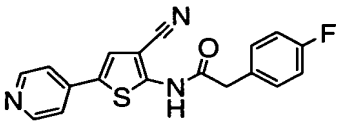
**I-A-4**



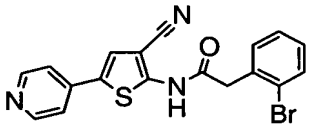
**I-A-5**



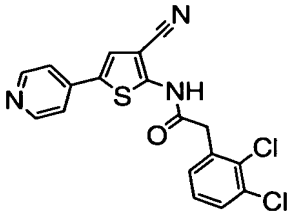
**I-A-6**



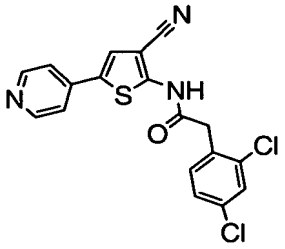

**I-A-7**



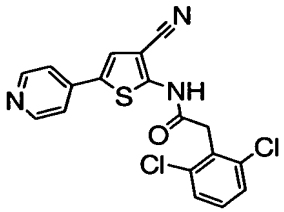

**I-A-8**



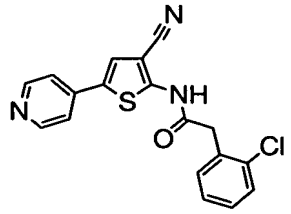

**I-A-9**



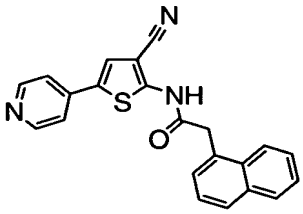

**I-A-10**



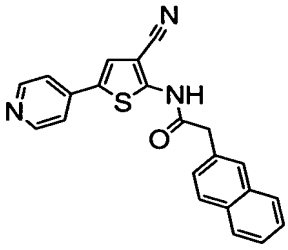

**I-A-11**



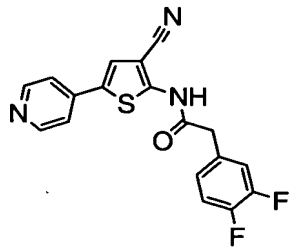

**I-A-12**



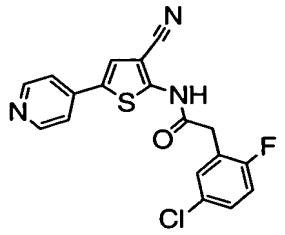

**I-A-13**



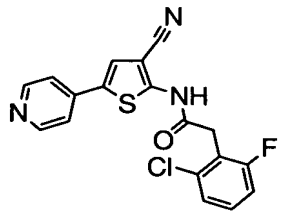

**I-A-14**



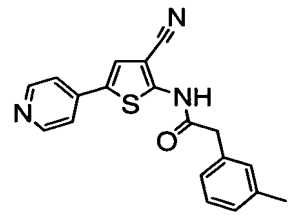

**I-A-15**



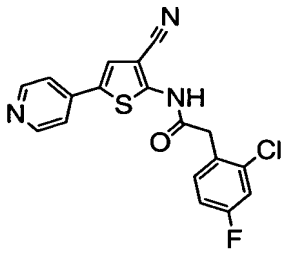

**I-A-16**



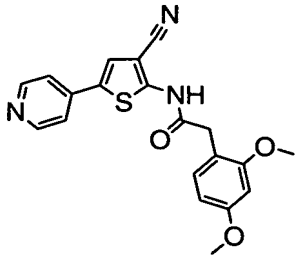

**I-A-17**



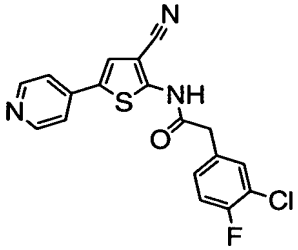

**I-A-18**



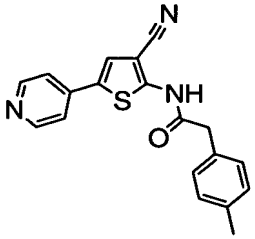
**I-A-19**



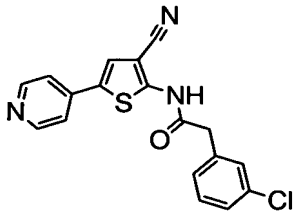
**I-A-20**



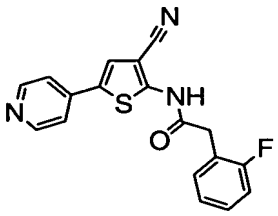
**I-A-21**



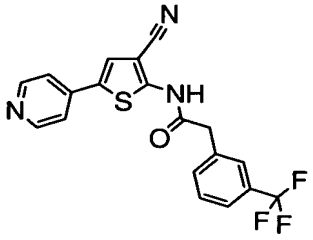
**I-A-22**



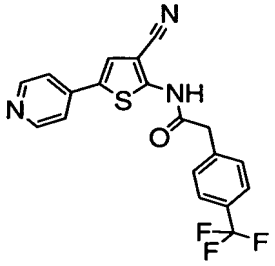
**I-A-23**



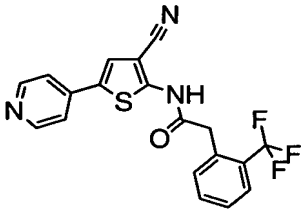
**I-A-24**



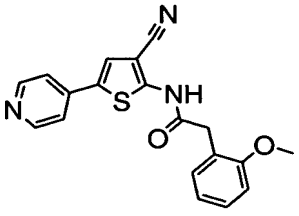
**I-A-25**



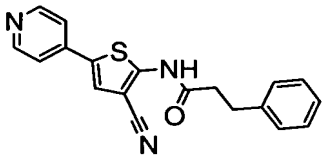
**I-A-26**



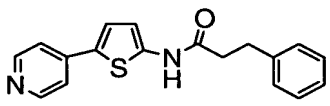
**I-A-27**



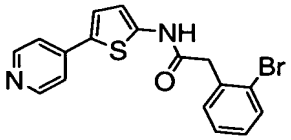
**I-A-28**



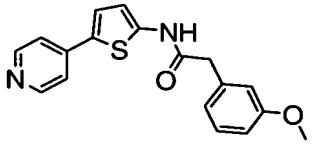
**I-A-29**



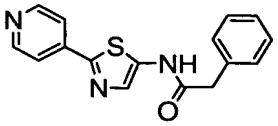
**I-A-30**



**I-A-31**



**I-A-32**



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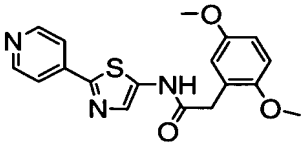

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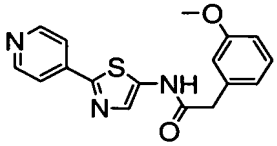

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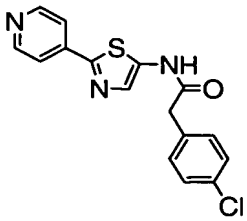

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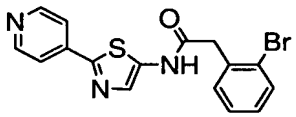

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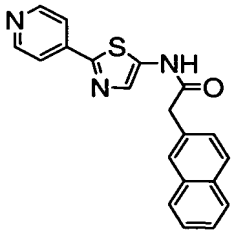

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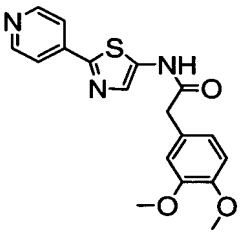

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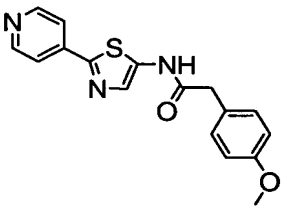

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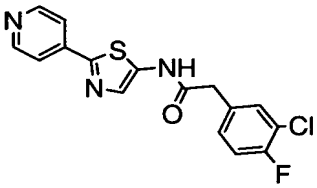

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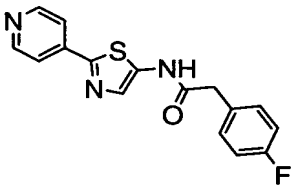

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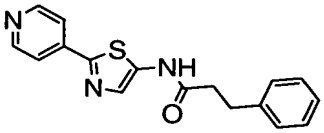

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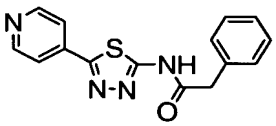

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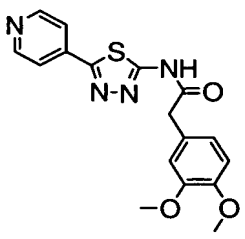

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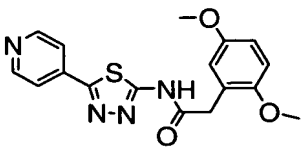

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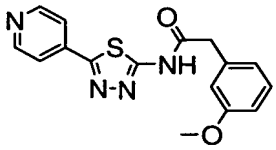

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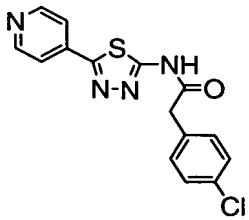

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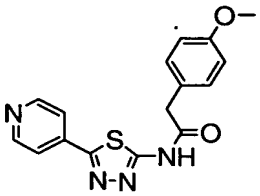

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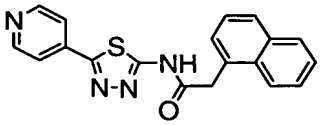

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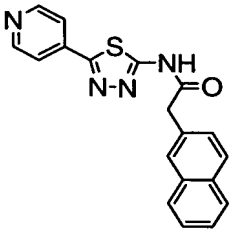

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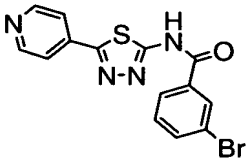

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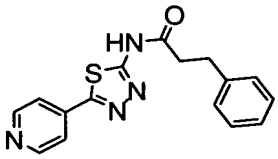

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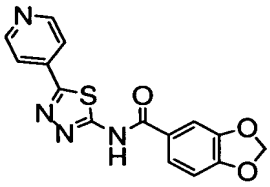

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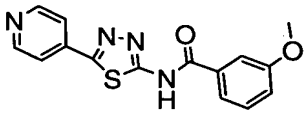

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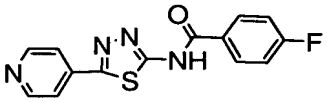

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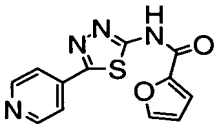

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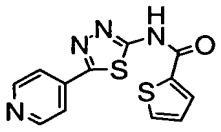

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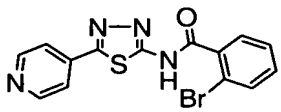

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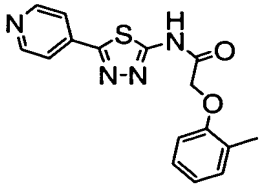

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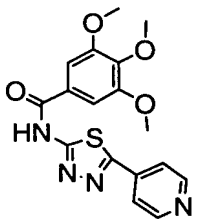

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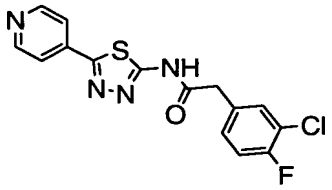

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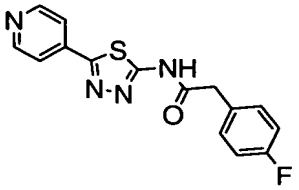

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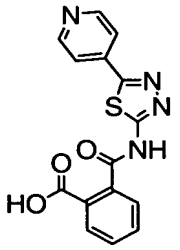

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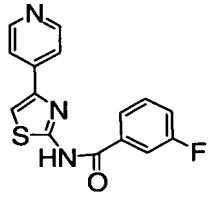

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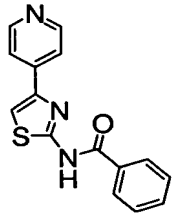

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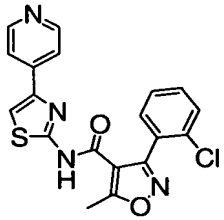

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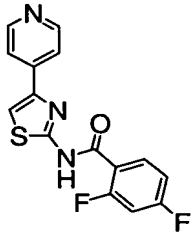

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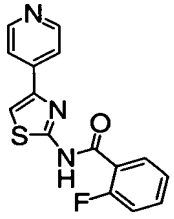

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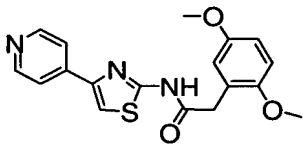

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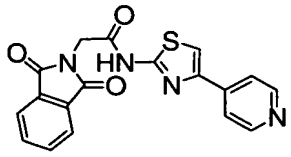

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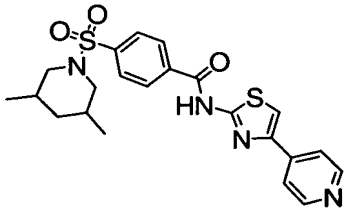

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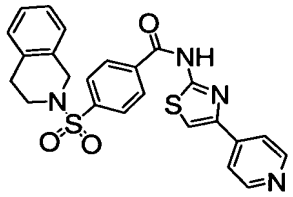

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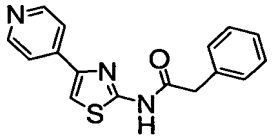

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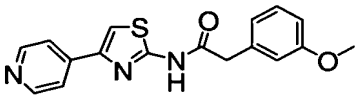

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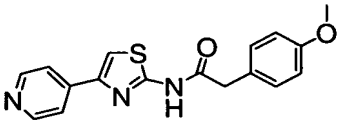

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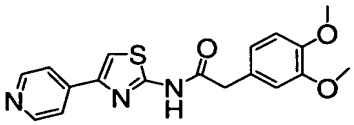

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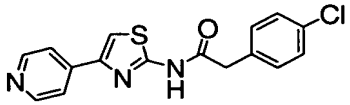

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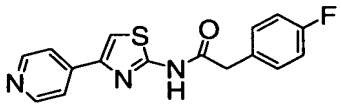

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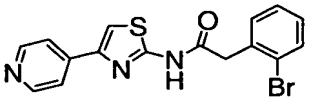

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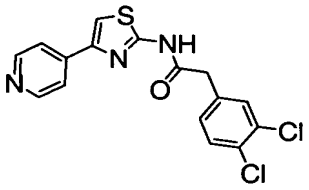

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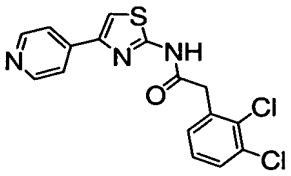

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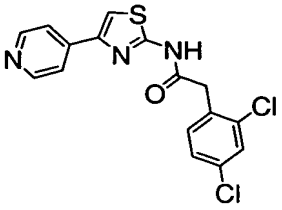

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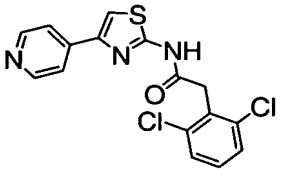

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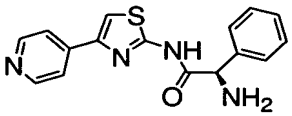

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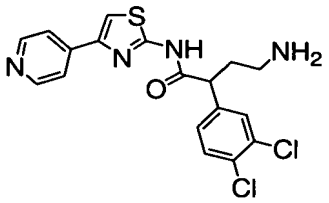

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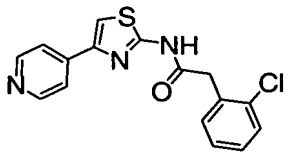

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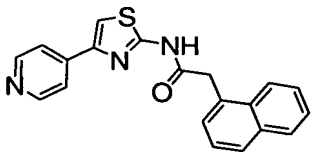

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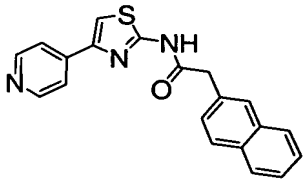

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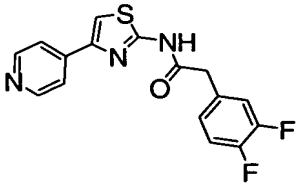
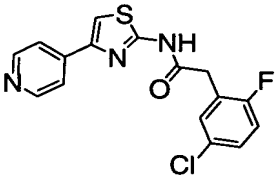


**I-B-35**



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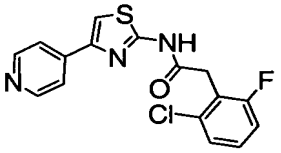

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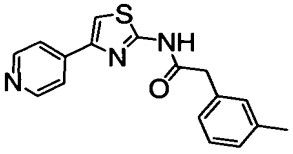

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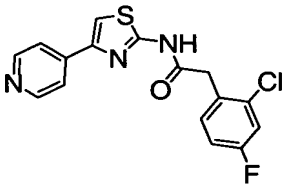

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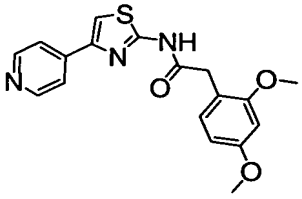

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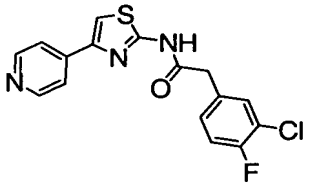

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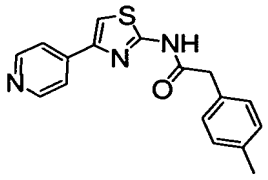

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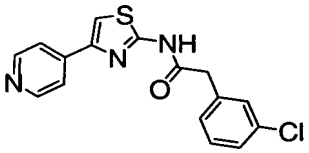

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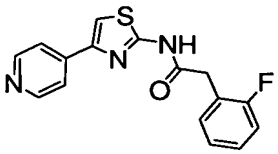

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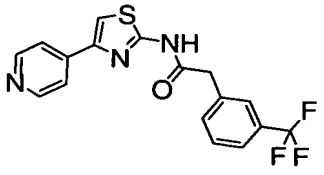

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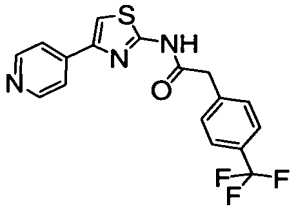

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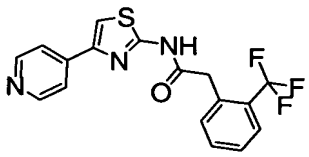

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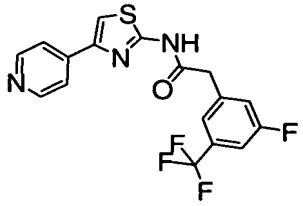

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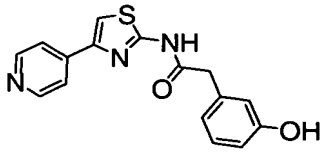

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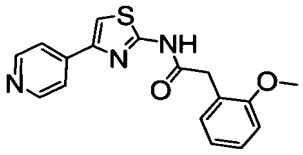

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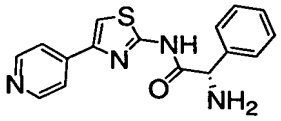

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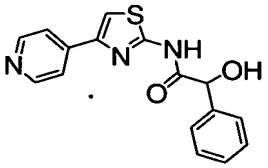

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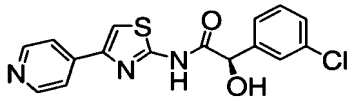

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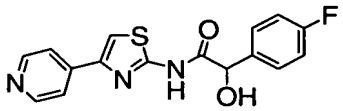

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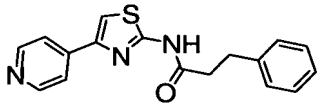

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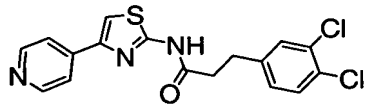

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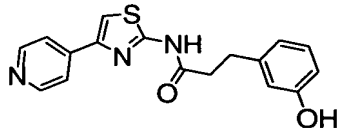

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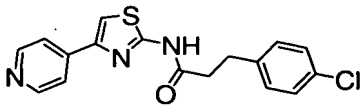

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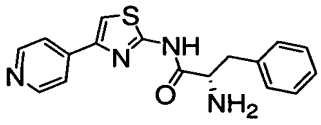

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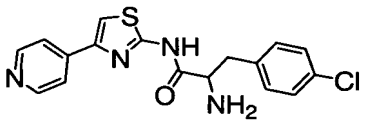

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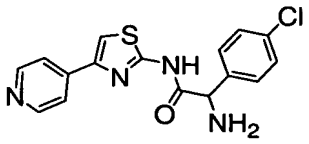

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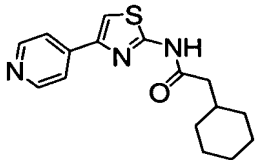

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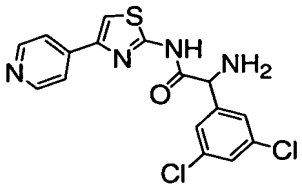

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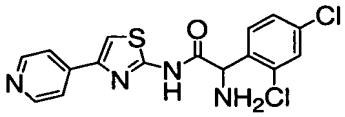

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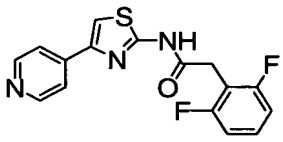

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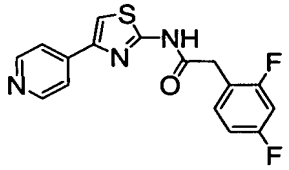

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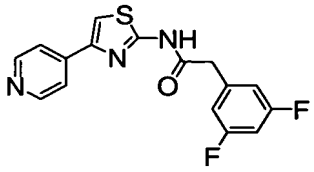

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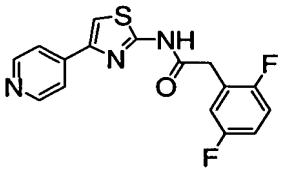

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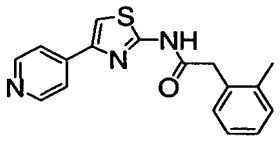

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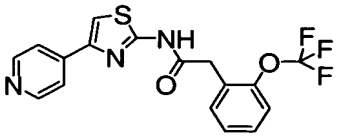

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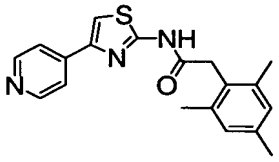

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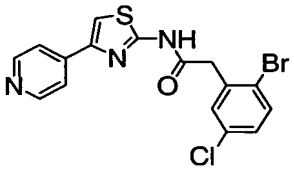

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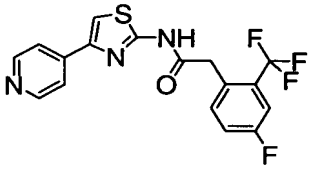

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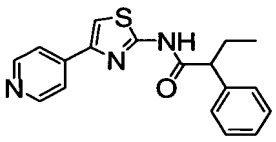

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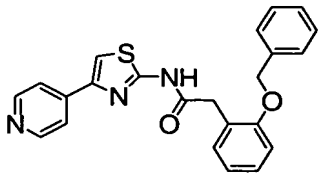

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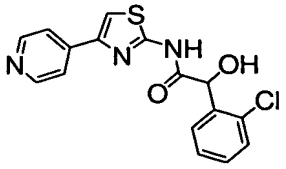

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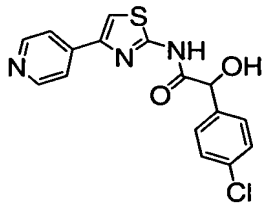

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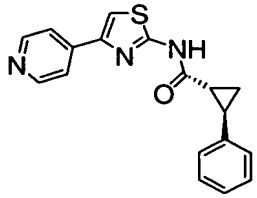

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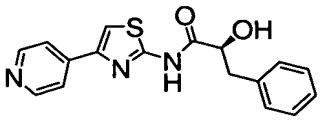

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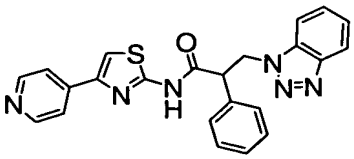

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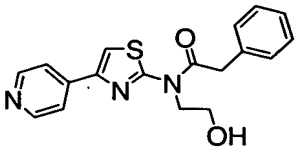

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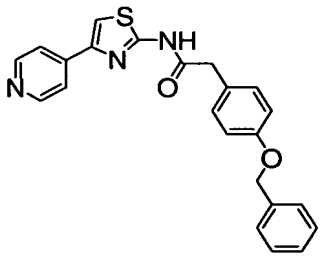

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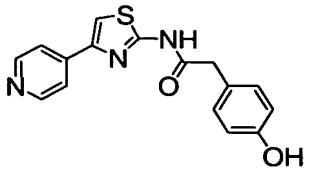

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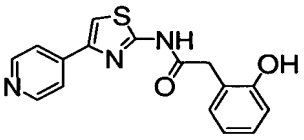

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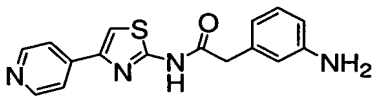

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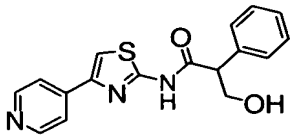

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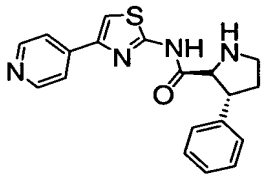

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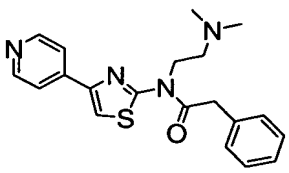

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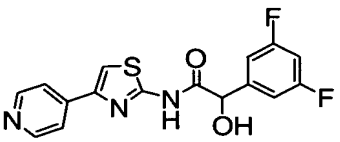

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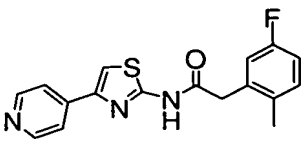

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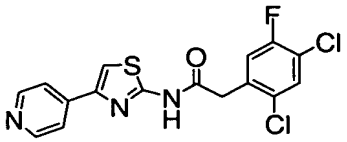

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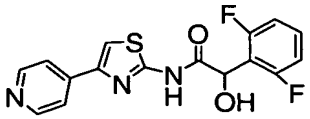

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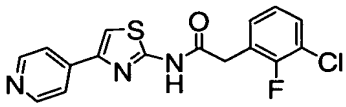

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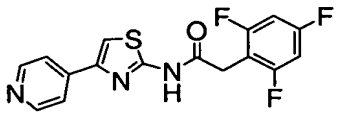

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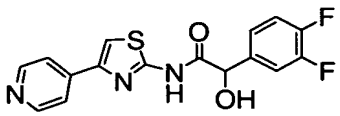

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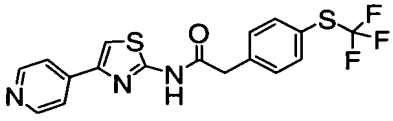

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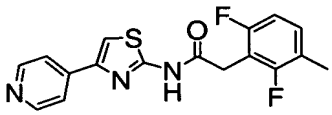

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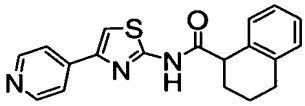

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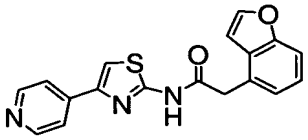

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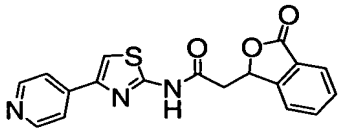

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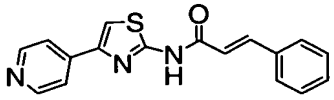

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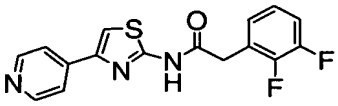

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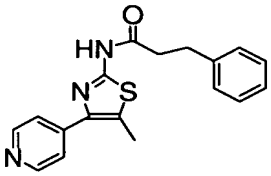

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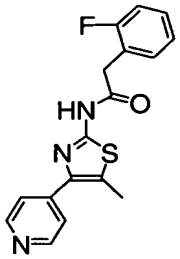

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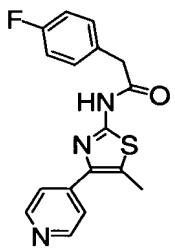

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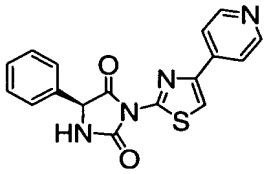

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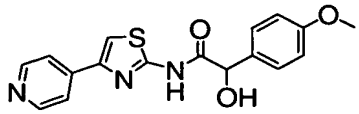

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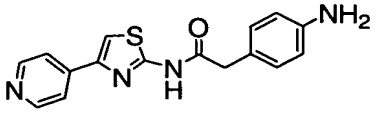

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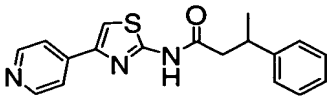

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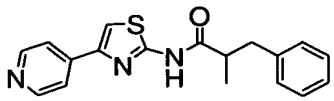

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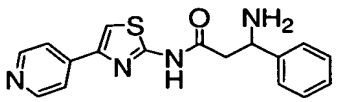

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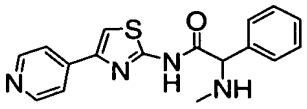

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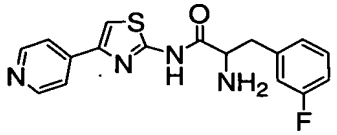

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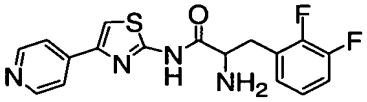

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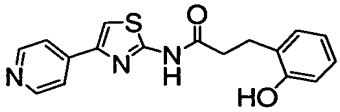

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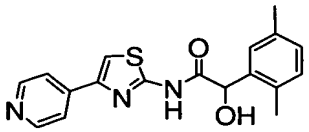

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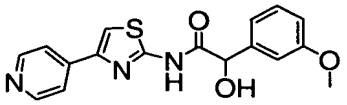

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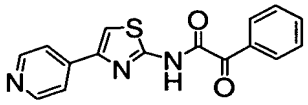

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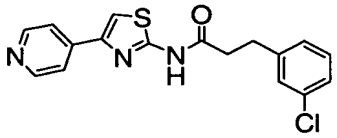

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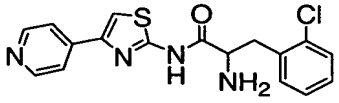

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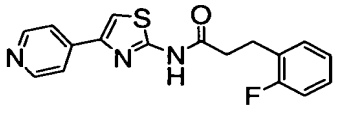

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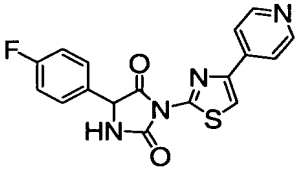

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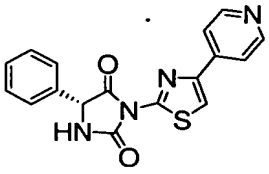

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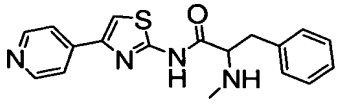

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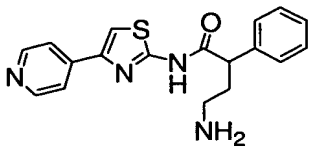

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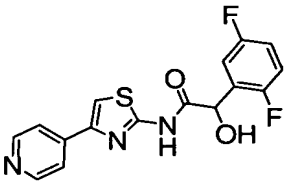

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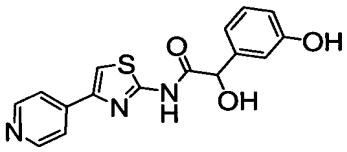

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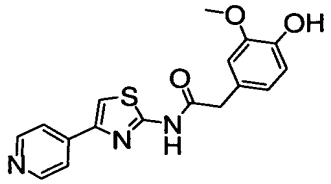

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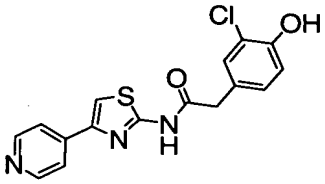

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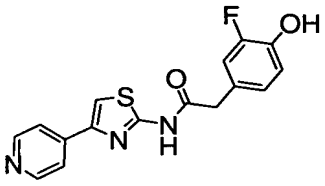

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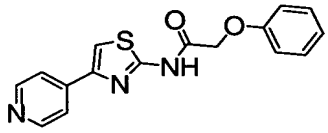

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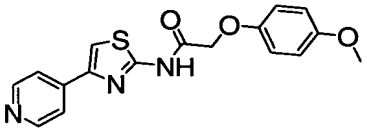

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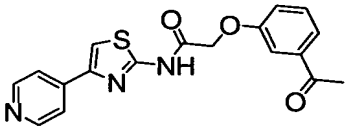

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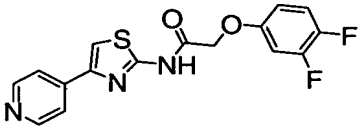

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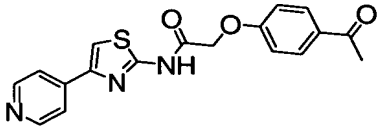

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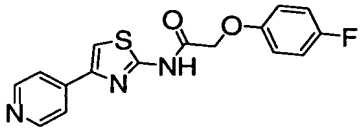

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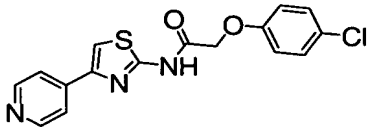

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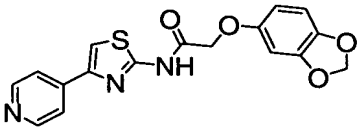

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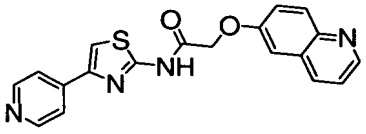

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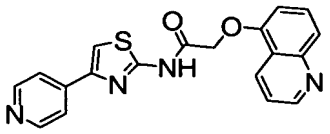

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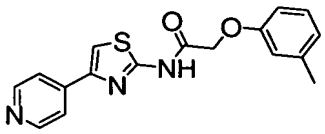

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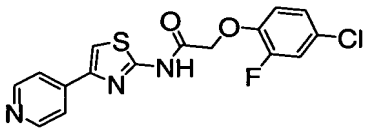

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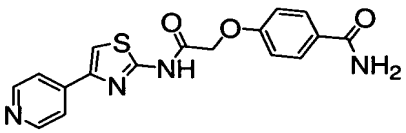

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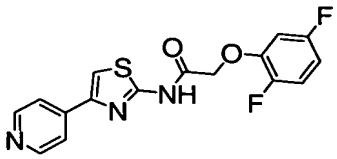

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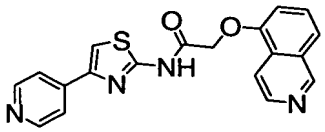

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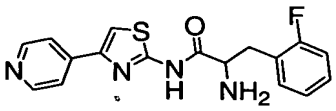

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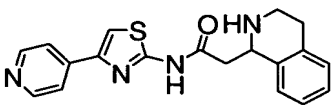

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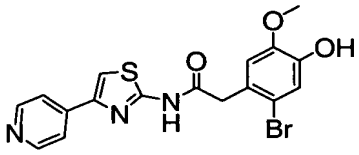

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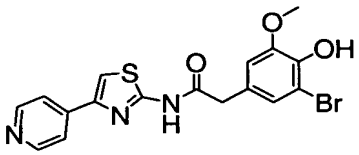

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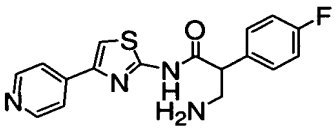

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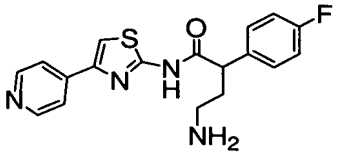
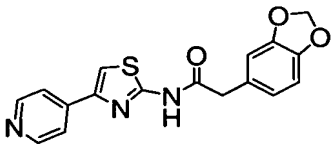


**I-B-151**



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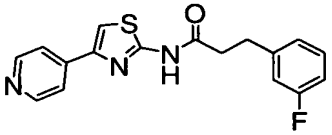

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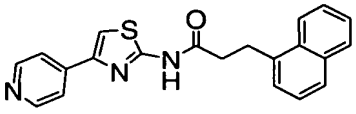

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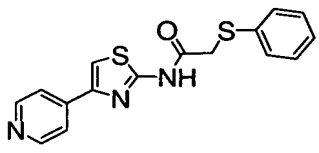

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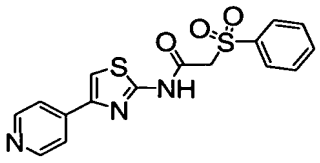

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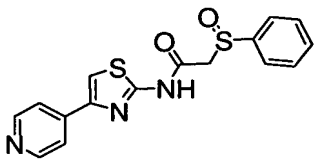

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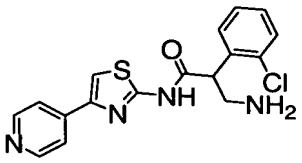

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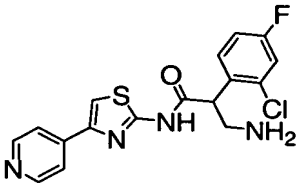

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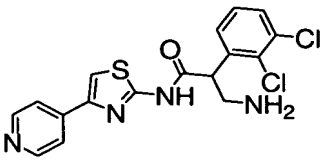

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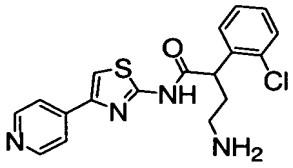

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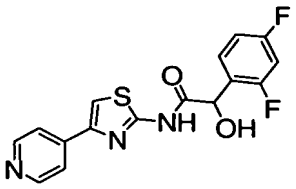

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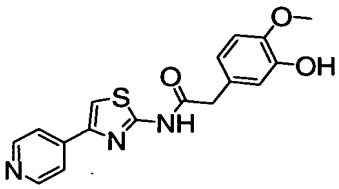

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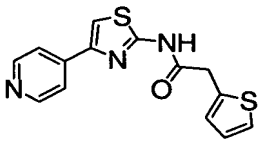

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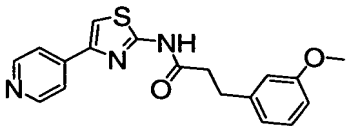

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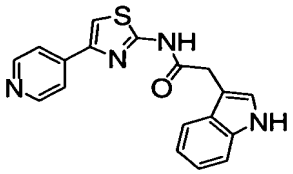

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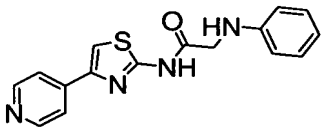

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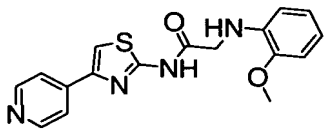

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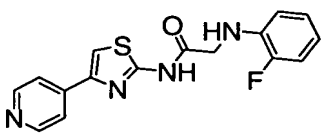

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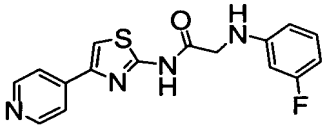

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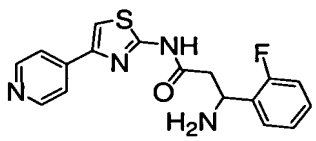

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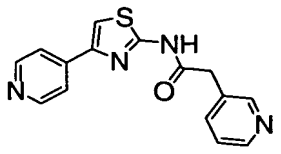

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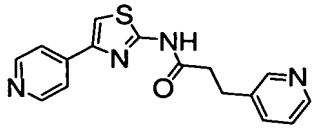

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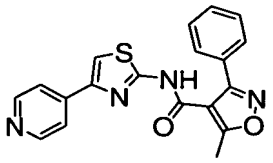

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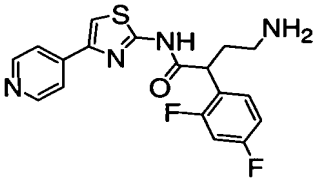

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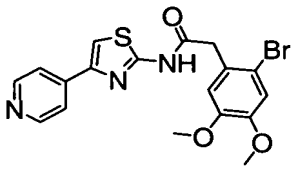

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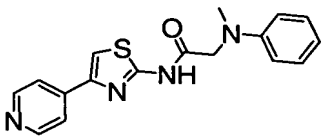

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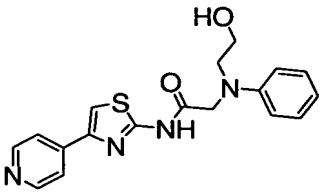

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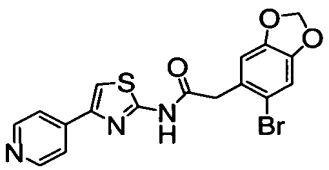

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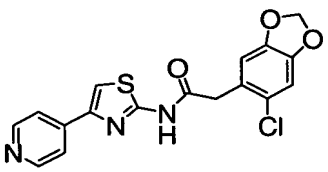

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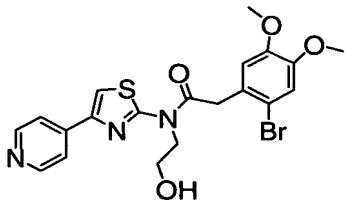

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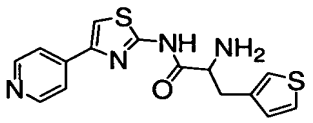

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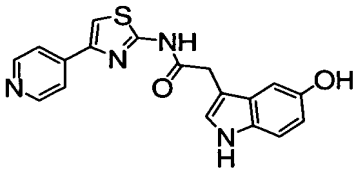

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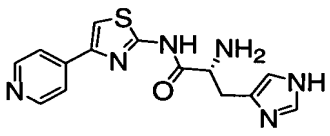

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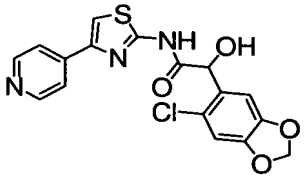

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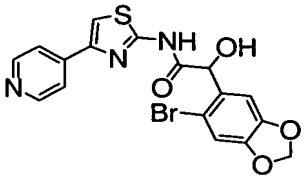

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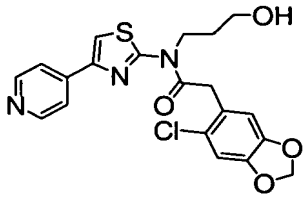

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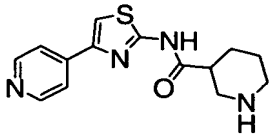

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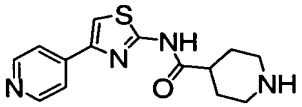

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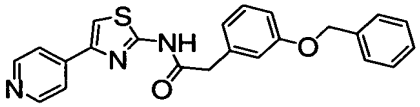

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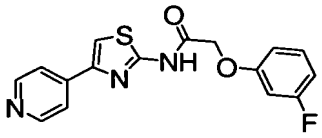

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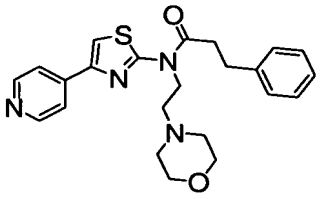

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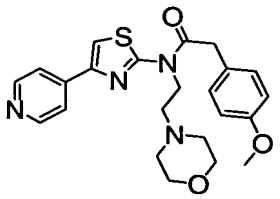

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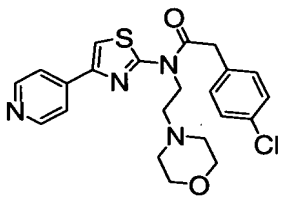

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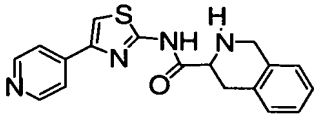

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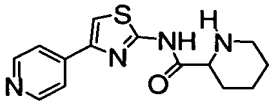

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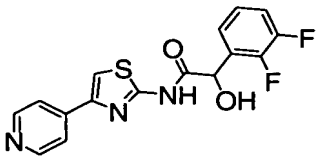

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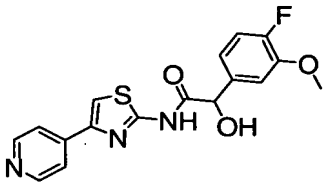

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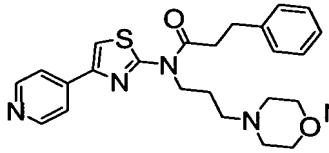

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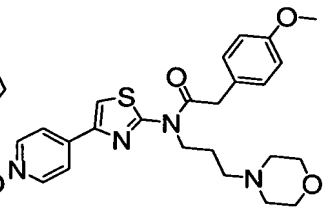

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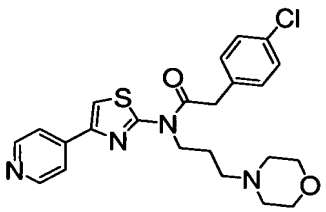

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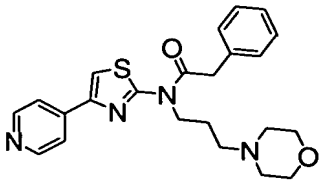

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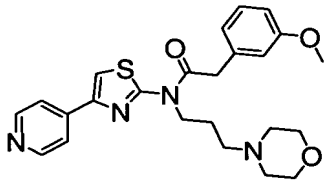

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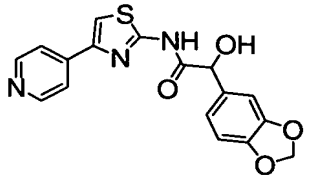

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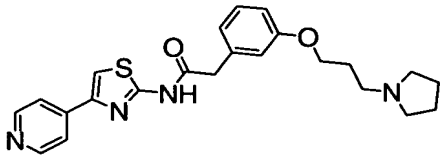

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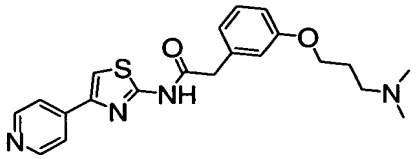

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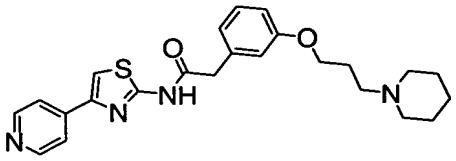

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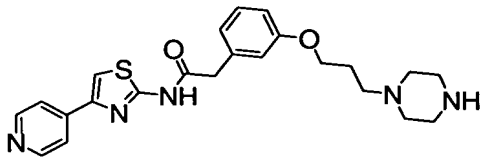

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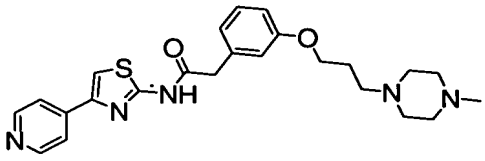
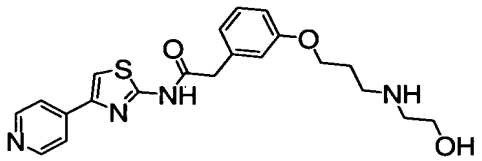


**I-B-209**



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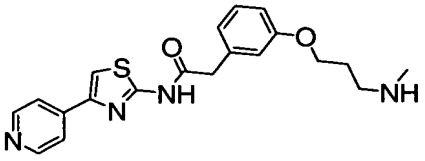

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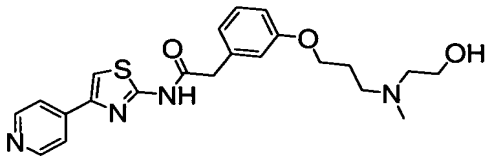

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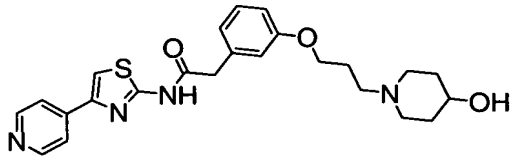

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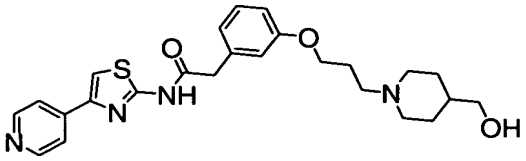

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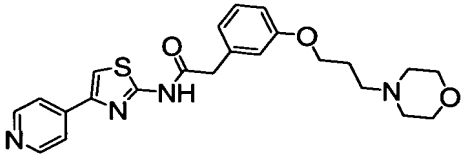

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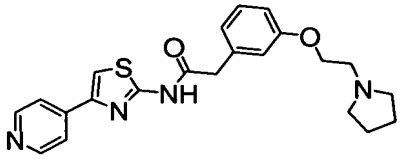

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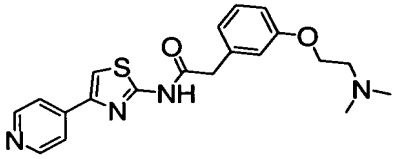

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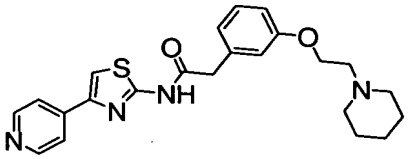

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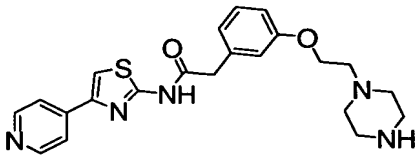

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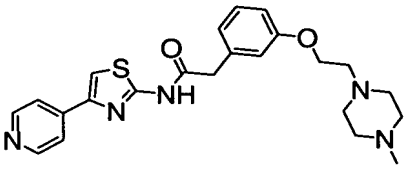

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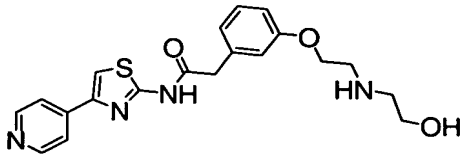

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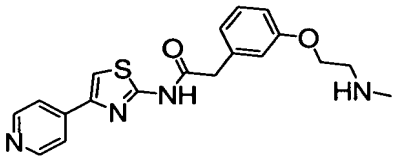

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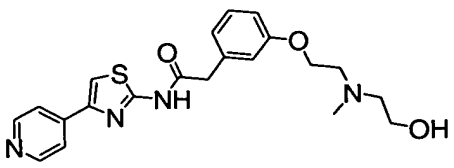

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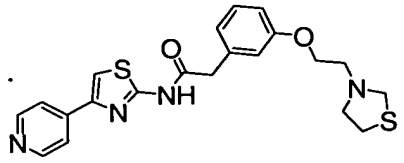

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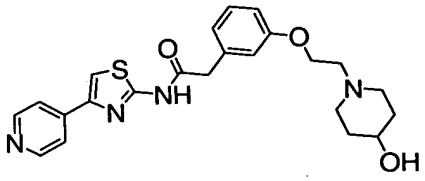

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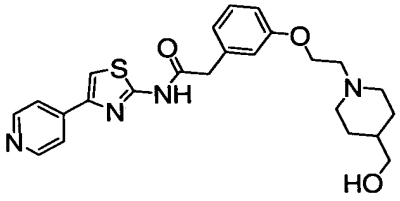

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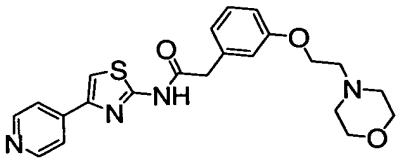

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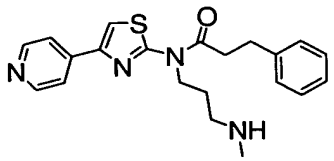

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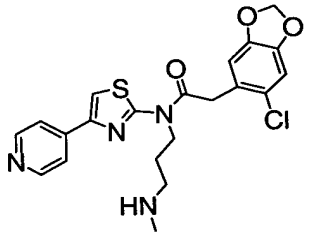

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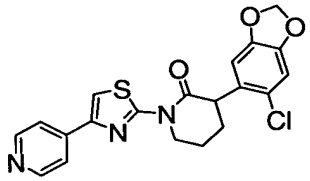

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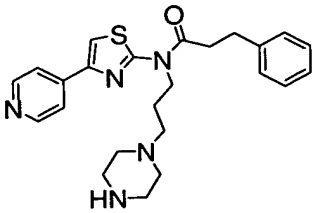

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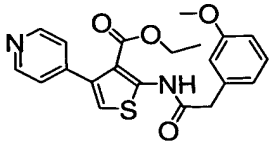

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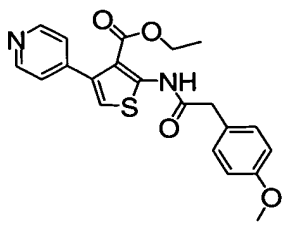

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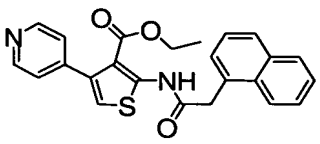

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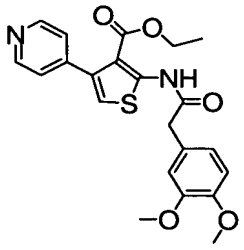

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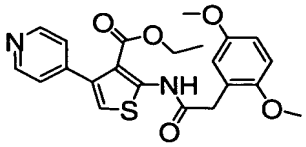

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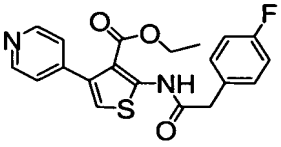

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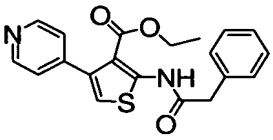

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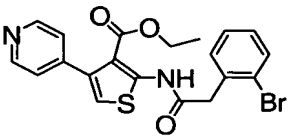

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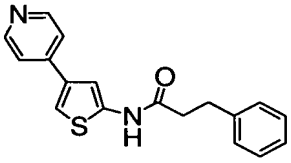

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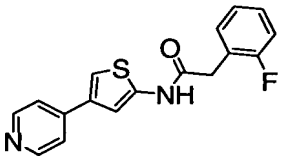

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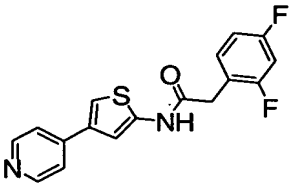

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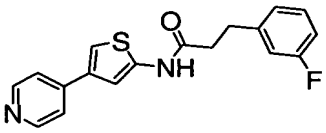

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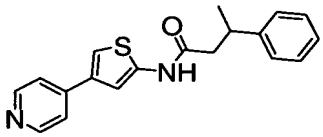

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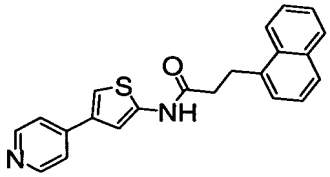

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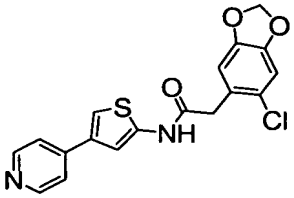

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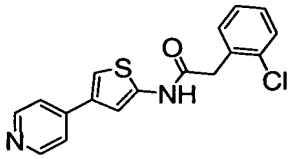

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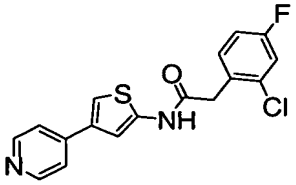

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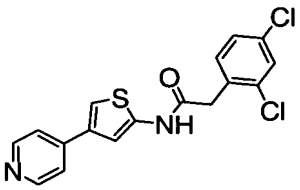

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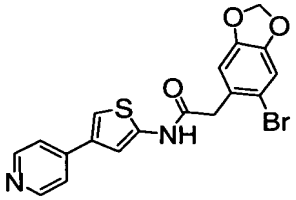

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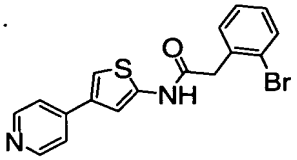

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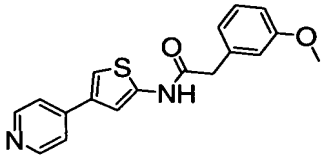

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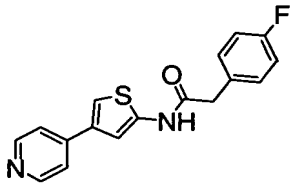

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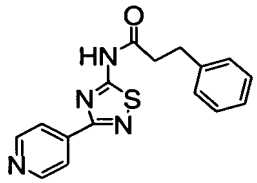

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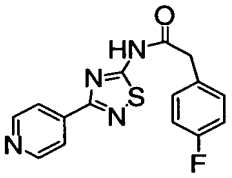

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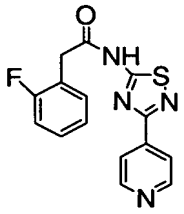

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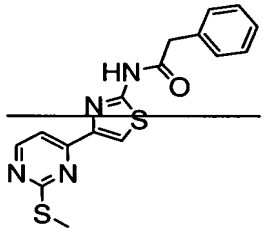

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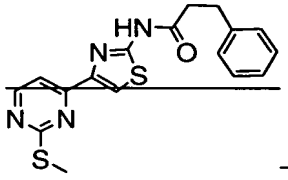

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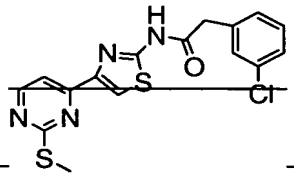

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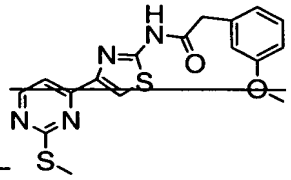

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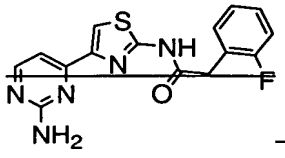

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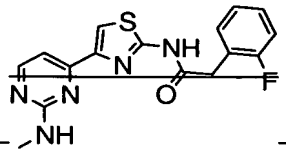

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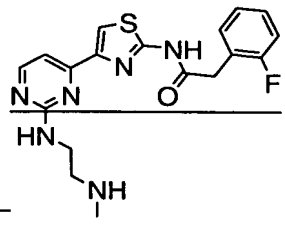

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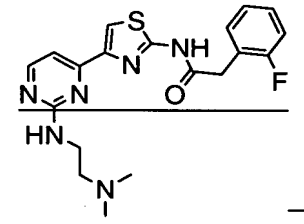

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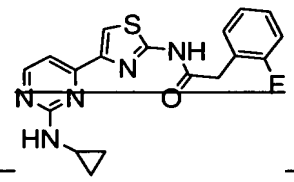

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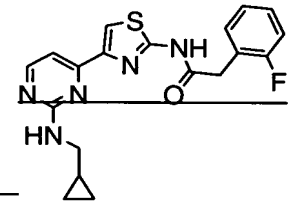

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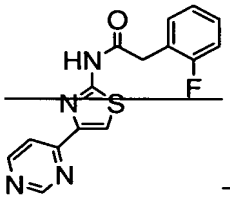

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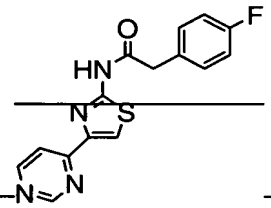

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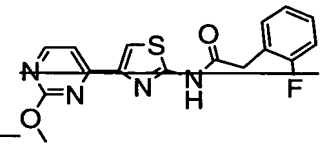

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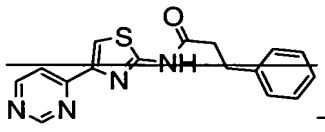

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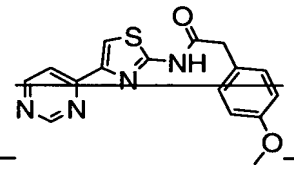

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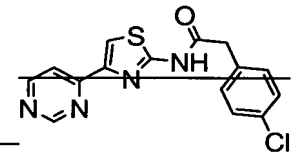

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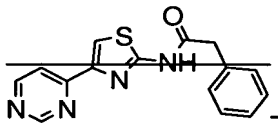

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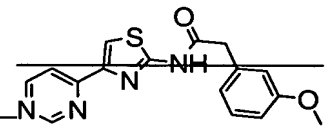

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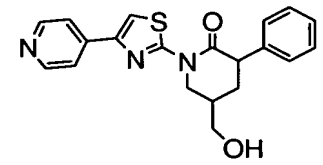
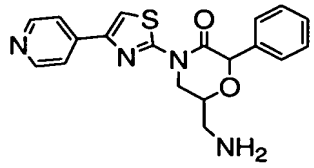
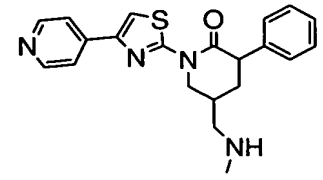


I-B-275



I-B-276



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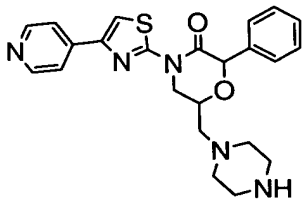

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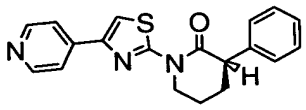

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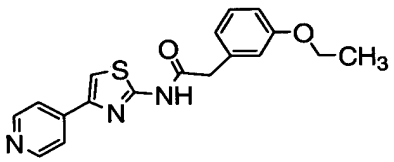

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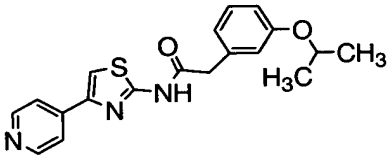

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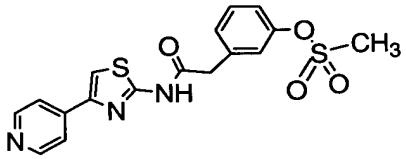

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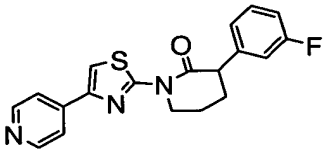

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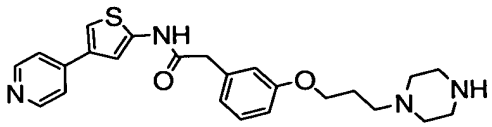

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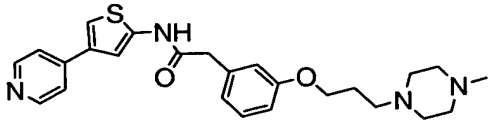

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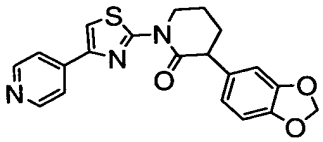

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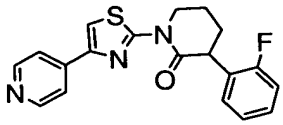

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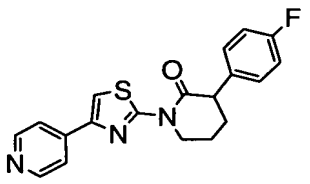

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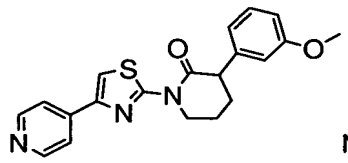

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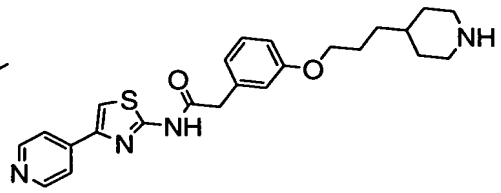

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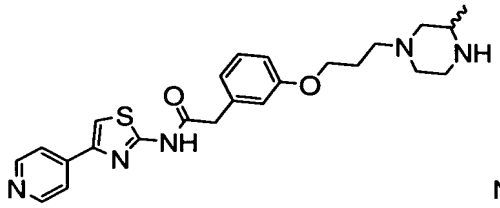

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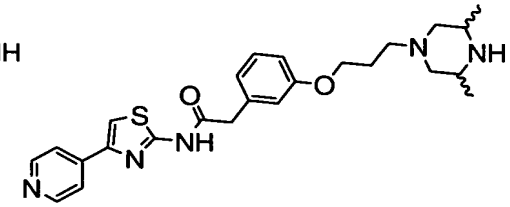

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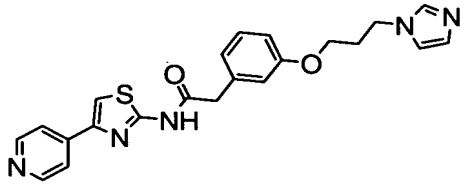

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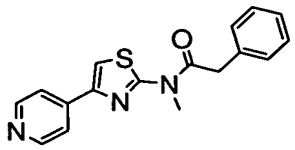

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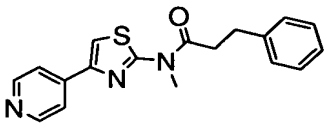

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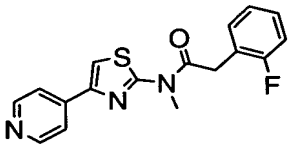

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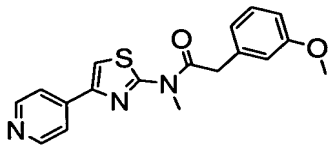

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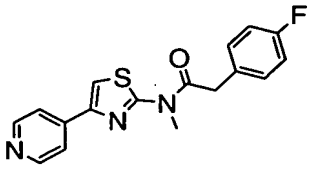

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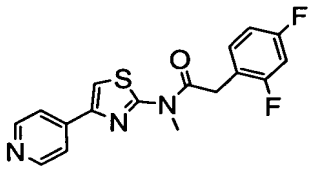

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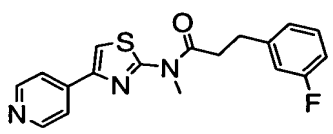

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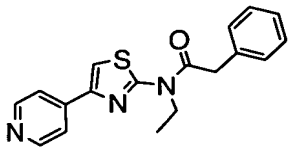

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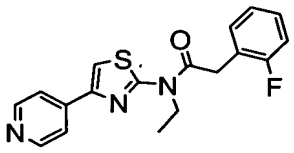

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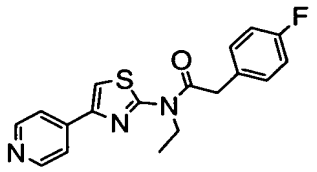

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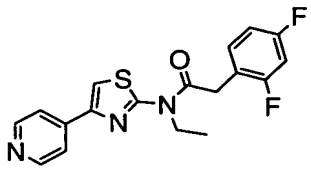

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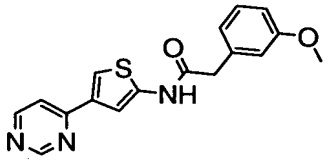

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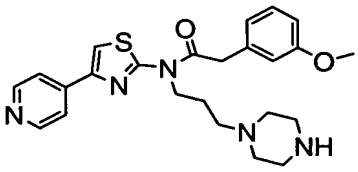

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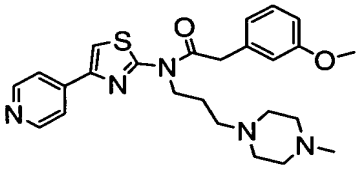

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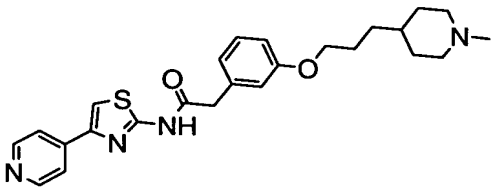

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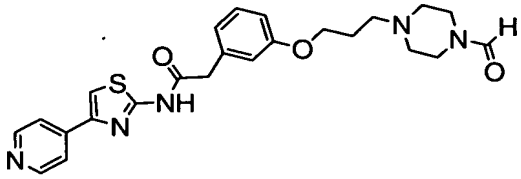

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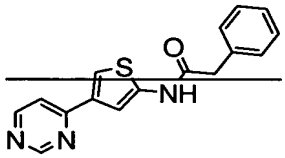

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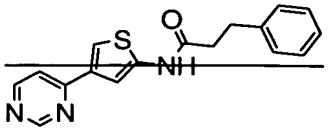

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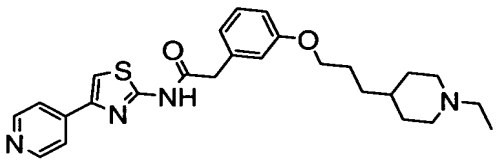

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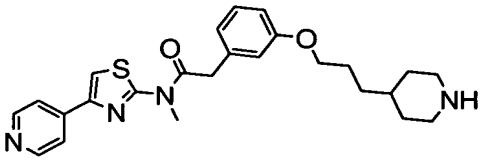

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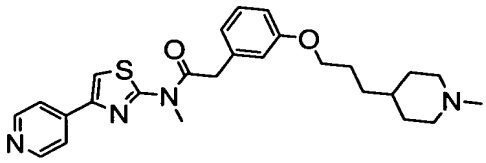

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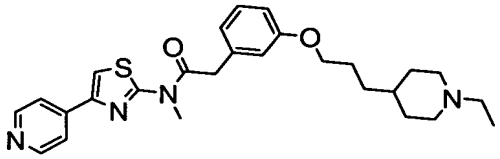

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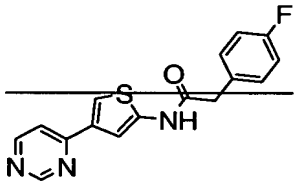

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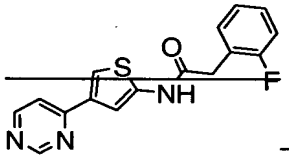

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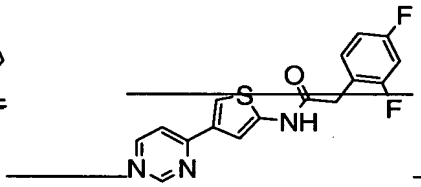

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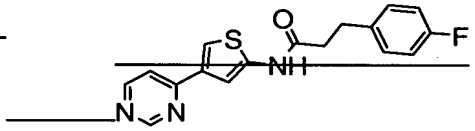

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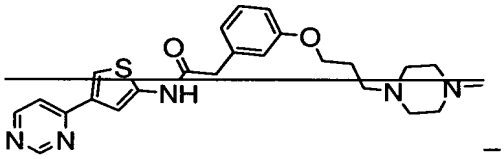

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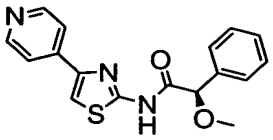

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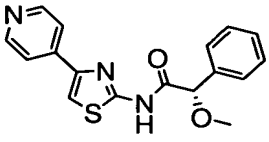

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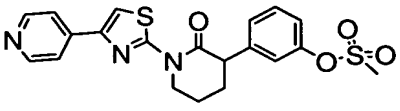

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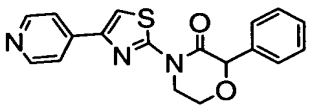

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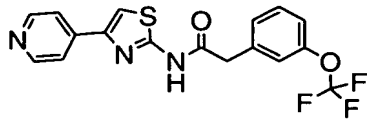
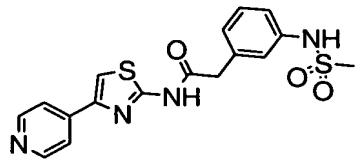


**I-B-325**



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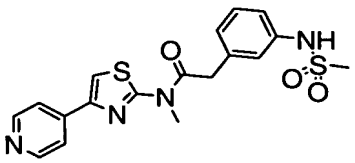

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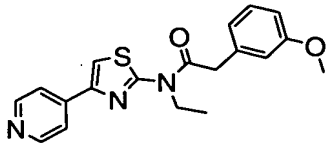

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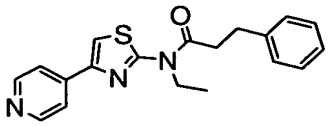

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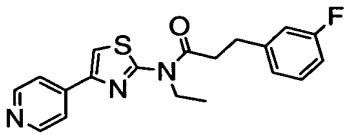

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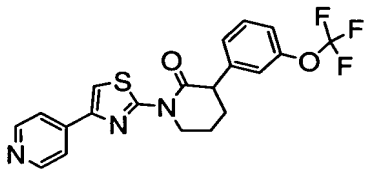

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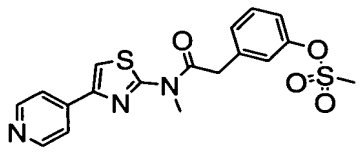

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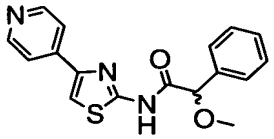

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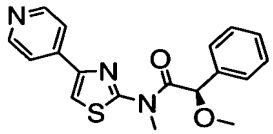

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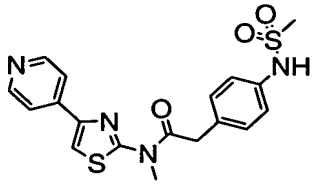

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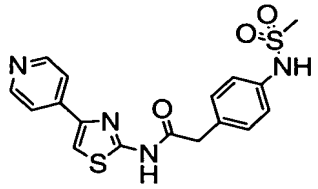

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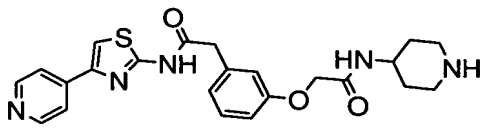

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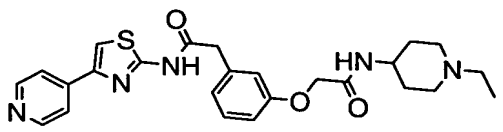

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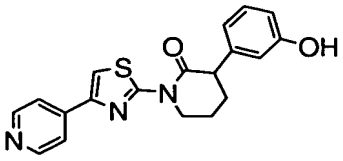

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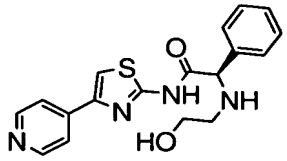

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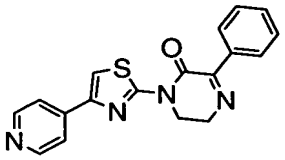

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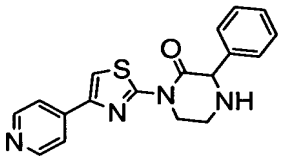

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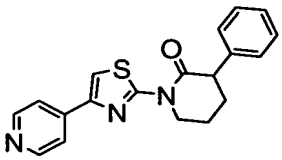

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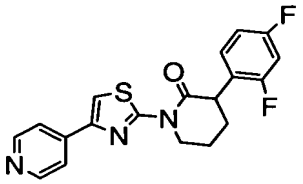

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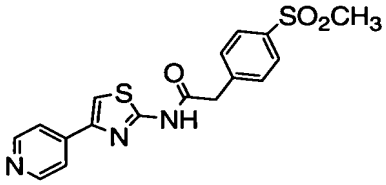

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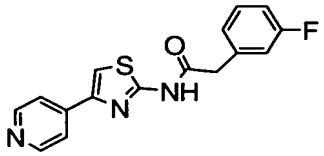

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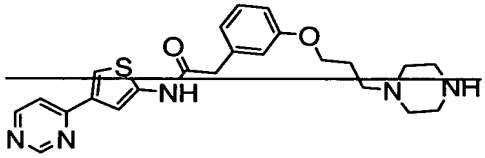

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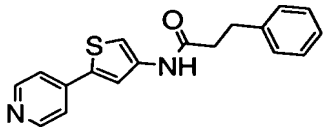
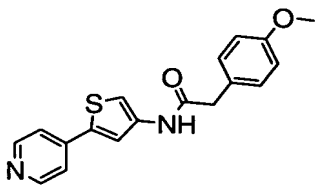


**I-C-1**



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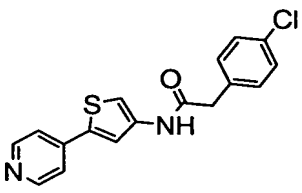

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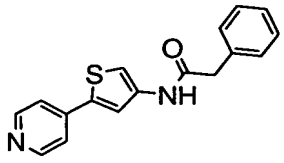

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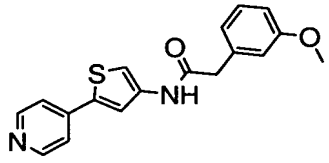

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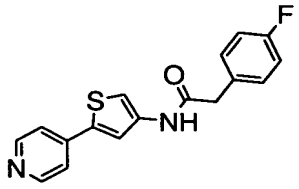

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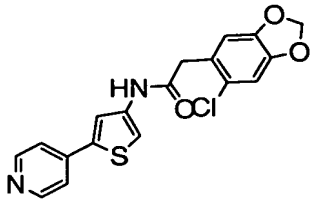

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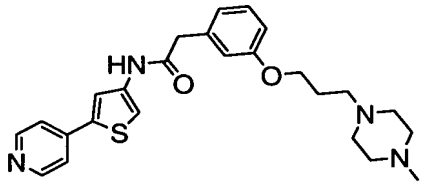

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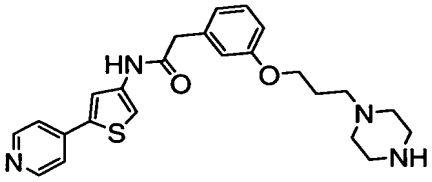

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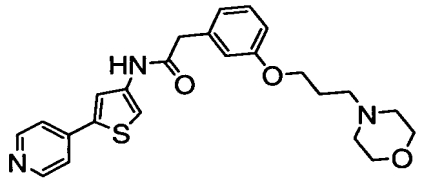

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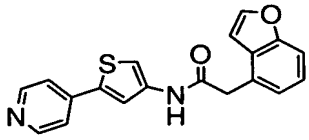

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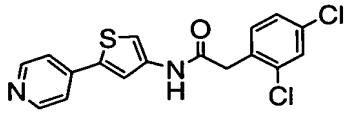

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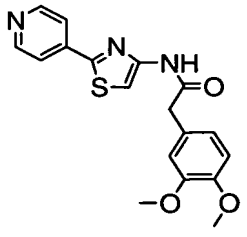

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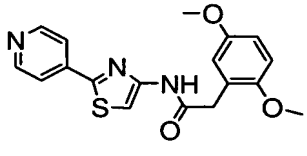

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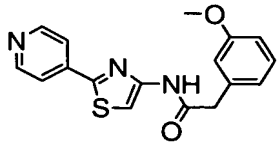

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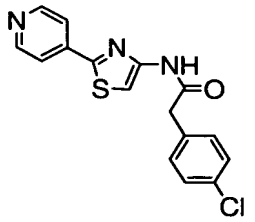

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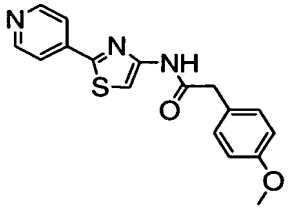

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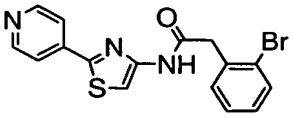

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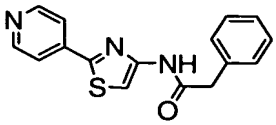

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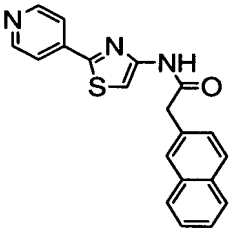

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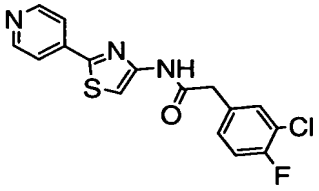

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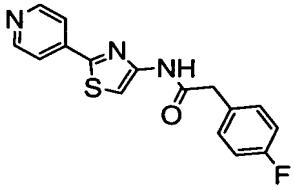

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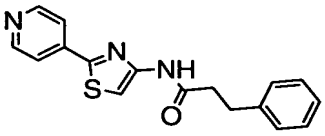

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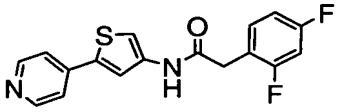

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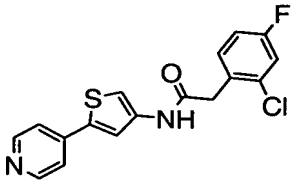

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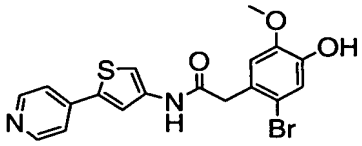

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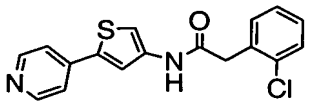

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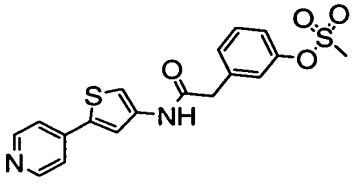

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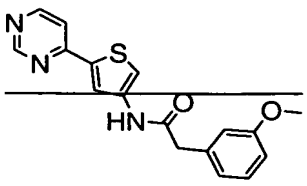

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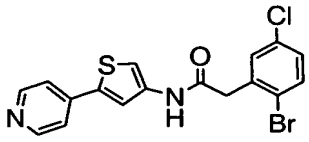

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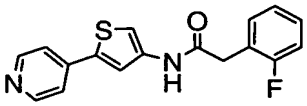
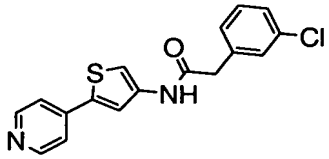
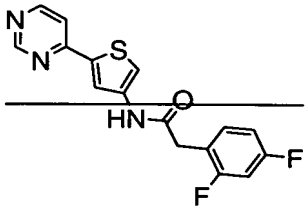


I-C-31



I-C-32



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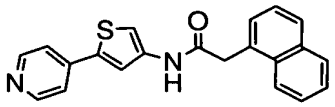
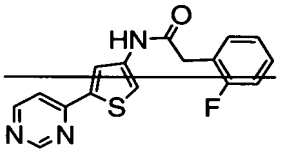


I-C-34



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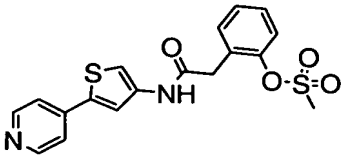
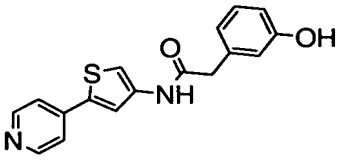
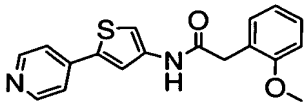


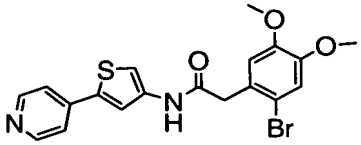
I-C-36



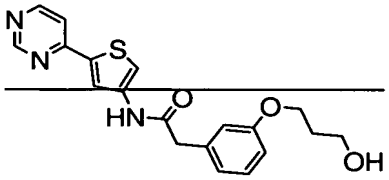
I-C-37



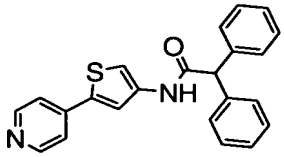
I-C-38



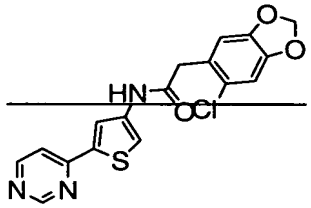
I-C-39



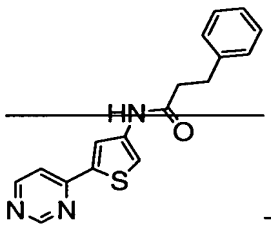
~~I-C-40~~



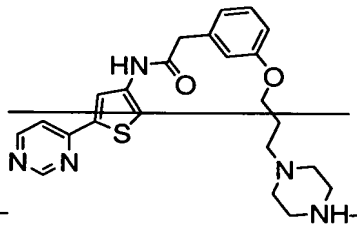
I-C-41



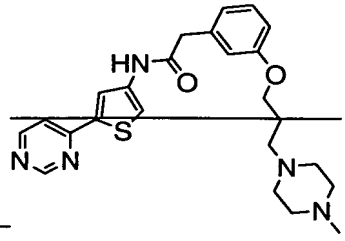
~~I-C-42~~



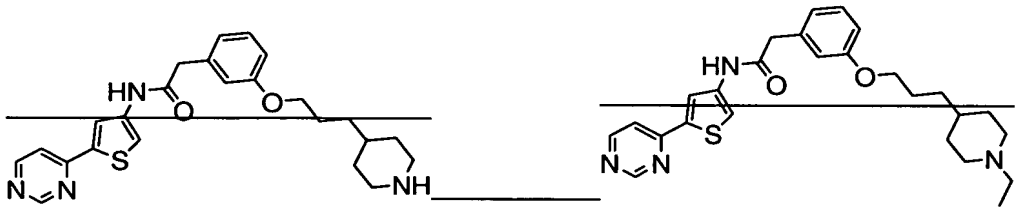
~~I-C-43~~



~~I-C-44~~



~~I-C-45~~



~~I-C-46~~ ~~I-C-47~~

46. (Original) A composition comprising an effective amount of compound of claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

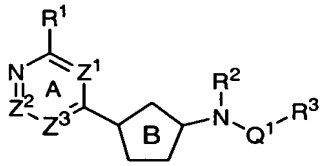
47. (Original) The composition of claim 46, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.

48. (Currently amended) A method of inhibiting ROCK, ERK, GSK, or AGC kinase activity in:

(a) a patient; or

(b) a biological sample;

which method comprises administering to said patient, or contacting said biological sample with a compound having the formula:



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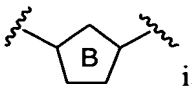
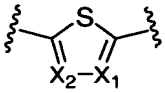
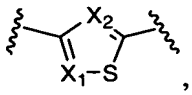
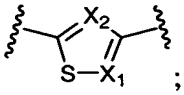
or a pharmaceutically acceptable salt thereof, wherein:

wherein  is  ,  , or  ;

$R^1$ is halogen, CN, $NO_2$, or $V_mR$;

$Z^1$ and $Z^3$ are each independently ~~N or~~ $CR^Z$, and $Z^2$ is ~~N or~~ $CR^1$~~, provided that Z1, Z2 and Z3 are not simultaneously N~~;

each occurrence of $R^Z$ is independently halogen, CN, $NO_2$, or $U_nR'$;

$R^2$ is $U_nR'$;

$X^1$ and $X^2$ are each independently $CR^4$ or N;

each occurrence of $R^4$ is independently halogen, CN, $NO_2$, or $V_mR$;

each occurrence of U or V is independently an optionally substituted $C_{1-6}$ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -$NRCO_2$-, -$SO_2NR$-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or -POR-;

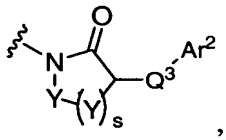
m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted $C_{1-6}$ aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted $C_{1-6}$ aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

$Q^1$ is –CO-, -$SO_2$-, -CONR-, or –$SO_2NR$-;

$R^3$ is $Q^2$-$Ar^1$,

or $R^2$ and $Q^1$-$R^3$, taken together with the nitrogen atom, form the cyclic group:



, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -$SO_2$-, -O-, -S-, -$NR^5$-, or -$C(R^5)_2$-, and $R^5$ is $U_nR'$;

$Q^2$ and $Q^3$ are each independently a bond or a $C_{1-6}$ alkylidene chain, wherein up to two

methylene units of the chain are each optionally and independently replaced by –NR'-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO-, -NR'$CO_2$-, -$SO_2$NR'-, -NR'$SO_2$-, -CONR'NR'-, -NR'CONR'-, -OCONR'-, -NR'NR'-, -NR'$SO_2$NR'-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or –POR'-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of $R^6$, wherein each occurrence of $R^6$ is independently halogen, CN, $NO_2$, or $U_nR'$, or two occurrences of $R^6$, or R' and $R^6$, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

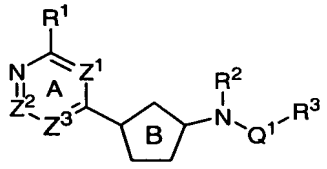
$Ar^1$ and $Ar^2$ are each independently a 5-8 membered saturated, partially unsaturated, or

fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein $Ar^1$ and $Ar^2$ are each optionally substituted with 0-5 independent occurrences of $TR^7$; wherein T is a bond or is a $C_1$-$C_6$ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NR$CO_2$-, -$SO_2$NR-, -NR$SO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NR$SO_2$NR-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or -POR-; and each occurrence of $R^7$ is independently R', halogen, $NO_2$, or CN;

or a pharmaceutically acceptable salt or composition thereof.

49. (Original) The method of claim 48, wherein the method comprises inhibiting ROCK activity.

50. (Currently amended) A method of treating or lessening the severity of a disease condition or disorder selected from a proliferative disorder, a cardiac disorder, a neurodegenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, a viral disease, or a bone disorder, comprising the step of administering to said patient a compound having the formula:



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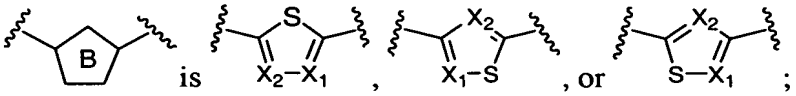
or a pharmaceutically acceptable salt thereof, wherein:

wherein  is ;

$R^1$ is halogen, CN, $NO_2$, or $V_mR$;

$Z^1$ and $Z^3$ are each independently ~~N or~~ $CR^Z$, and $Z^2$ is ~~N or~~ $CR^1$~~, provided that Z1, Z2 and Z3 are not simultaneously N~~;

each occurrence of $R^Z$ is independently halogen, CN, $NO_2$, or $U_nR'$;

$R^2$ is $U_nR'$;

$X^1$ and $X^2$ are each independently $CR^4$ or N;

each occurrence of $R^4$ is independently halogen, CN, $NO_2$, or $V_mR$;

each occurrence of U or V is independently an optionally substituted $C_{1-6}$ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -

CONR-, -NRCO-, -$NRCO_2$-, -$SO_2NR$-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or -POR-;

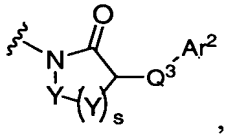
m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted $C_{1-6}$ aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted $C_{1-6}$ aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

$Q^1$ is –CO-, -$SO_2$-, -CONR-, or –$SO_2NR$-;

$R^3$ is $Q^2$-$Ar^1$,

or $R^2$ and $Q^1$-$R^3$, taken together with the nitrogen atom, form the cyclic group:




, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -$SO_2$-, -O-, -S-, -$NR^5$-, or -$C(R^5)_2$-, and $R^5$ is $U_nR'$;

$Q^2$ and $Q^3$ are each independently a bond or a $C_{1-6}$ alkylidene chain, wherein up to two

methylene units of the chain are each optionally and independently replaced by –NR'-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO-, -NR'$CO_2$-, -$SO_2$NR'-, -NR'$SO_2$-, -CONR'NR'-, -NR'CONR'-, -OCONR'-, -NR'NR'-, -NR'$SO_2$NR'-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or –POR'-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of $R^6$, wherein each occurrence of $R^6$ is independently halogen, CN, $NO_2$, or $U_nR'$, or

two occurrences of $R^6$, or R' and $R^6$, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

$Ar^1$ and $Ar^2$ are each independently a 5-8 membered saturated, partially unsaturated, or

fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein $Ar^1$ and $Ar^2$ are each optionally substituted with 0-5 independent occurrences of $TR^7$; wherein T is a bond or is a $C_1$-$C_6$ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -$CO_2$-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -$NRCO_2$-, -$SO_2NR$-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, -$SO_2$-, -PO-, -$PO_2$-, or -POR-; and each occurrence of $R^7$ is independently R', halogen, $NO_2$, or CN;

or a pharmaceutically acceptable salt or composition thereof.

51. (Original) The method of claim 50, comprising the additional step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an anti-psychotic agent, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and

said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.

52. (Original) The method of claim 50, wherein disease, condition, or disorder is allergy, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (AML, Lou Gehrig's disease), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusion/ischemia (e.g., stroke), baldness, cancer, hepatomegaly, cardiovascular disease including cardiomegaly, cystic fibrosis, viral disease, autoimmune diseases, atherosclerosis, restenosis, psoriasis, inflammation, hypertension, angina pectoris, cerebrovascular contraction, peripheral circulation disorder, premature birth, arteriosclerosis, vasospasm (cerebral vasospasm, coronary vasospasm), retinopathy, erectile dysfunction (ED), AIDS, osteoporosis, Crohn's Disease and colitis, neurite outgrowth, or Raynaud's Disease.

53. (Original) The method of claim 50, wherein disease, condition, or disorder is atherosclerosis, hypertension, erectile dysfunction (ED), reperfusion/ischemia (e.g., stroke), or vasospasm (cerebral vasospasm and coronary vasospasm).